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ABSTRACT BOOK

**47th World Conference
on Lung Health of the
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Tuberculosis and Lung Disease (The Union)**

**LIVERPOOL • UNITED KINGDOM
26-29 OCTOBER 2016**

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The International Journal of Tuberculosis and Lung Disease

The Official Journal of the International Union Against Tuberculosis and Lung Disease

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47th World Conference on Lung Health of the International Union Against Tuberculosis and Lung Disease (The Union) Liverpool, UK, 26–29 October 2016

SYMPOSIA: THURSDAY 27 OCTOBER 2016

01. High-dose rifampicin: recovering an old drug in the post-multidrug-resistant TB era

High-dose rifampicin in pulmonary TB

G Davies¹ ¹University of Liverpool, Liverpool, UK. e-mail: gerrydavies@doctors.org.uk

Early dosing recommendations for rifampicin were based largely on cost considerations. Current efforts to re-evaluate dosing of rifampicin are aimed at improving efficacy by increasing doses, based on promising results in in vivo models. We will report the results of two pharmacokinetic-pharmacodynamics studies that assessed exposure, efficacy, and safety of current formulations of rifampicin at 1.5 and 2 times standard doses. Results will be pooled across the two studies HIRIF and HIGHRIF2, conducted respectively in Peru and Tanzania, to increase the power to detect differences in safety and efficacy endpoints and to increase the generalizability of findings. These results will be discussed in the context of other rifampicin-optimization efforts and plans for a Phase III trial of shorter rifampicin-based treatment.

Drug-drug interactions with rifampicin and implications for its use with new anti-TB drugs and in HIV-coinfected TB patients

K Dooley¹ ¹Johns Hopkins University, Baltimore, MD, USA. e-mail: kdooley1@jhmi.edu

Description: Rifampicin has unique activity against semi-dormant ‘persisters’. To date, no drug has proven sterilizing activity equal to that of rifamycins. There is a clear relationship between drug exposure and microbiologic activity; thus, high dose rifampicin holds promise for treatment shortening. However, rifampicin is a potent inducer of drug metabolizing enzymes and drug transporters, and rifampicin can reduce concentra-

tions of companion anti-TB drugs and drugs used to treat common comorbidities, such as HIV infection or diabetes mellitus. In this talk, the speaker will present current knowledge about clinically-meaningful drug interactions with rifampicin, the potential impact that higher rifampicin doses may have on metabolic drug interactions, and, how these interactions influence TB regimen development and the overall goal of developing treatments that will benefit all patients.

High-dose rifampicin in TB-meningitis

R Aarnoutse¹ ¹Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands. e-mail: rob.aarnoutse@radboudumc.nl

Tuberculous meningitis (TBM) is the most severe form of tuberculosis, resulting in death or neurological disability in 50% of patients. Rifampicin is pivotal in the treatment of TBM as shown by the high mortality in patients with rifampicin-resistant TBM, but the penetration of this drug into cerebral spinal fluid is limited. A small clinical trial on high dose, intravenously administered rifampicin showed a strong decrease in mortality in patients with TBM, but a large trial with a moderate rifampicin dose increase showed no benefit. Several pharmacokinetic studies are ongoing. This presentation will provide an overview of data on efficacy, safety/tolerability and pharmacokinetics of higher doses of rifampicin in adults and children with TBM. The merits of other TB drugs as alternatives to rifampicin, means of enhancing delivery of TB drugs into the central nervous system, and the way forward will be discussed.

Adjunctive therapies and other approaches to extending the useful life of rifampicin

T Gumbo¹ ¹Baylor Institute of Immunology Research, Dallas, TX, USA. e-mail: tawanda.gumbo@bswhealth.org

Based on pharmacokinetic/pharmacodynamic studies, simulations, and clinical data, we have proposed lowering the rifampicin susceptibility breakpoints from current 1 mg/L to 0.125 mg/L. This could increase numbers of patients with rifampicin-resistance by up to four-fold. In the hollow fiber system and in clinical studies, artificial intelligence algorithms have also identified AUCs and peak/MICs above which microbial

kill can be effected. We have also identified efflux pump induction and mutations central to rifampicin resistance, even in the presence of *rpoB* mutations. These can be overcome by use of a three step program: 1) Bayesian-feedback optimized dosing that achieves concentrations above the PK/PD target thresholds, 2) use of efflux pump inhibitors to lower the MIC and disrupt the 'antibiotic resistance arrow of time' in conjunction with step 1, and 3) enhancing the intracellular concentration of the rifampicin. Computer-aided clinical trial simulations will be presented to demonstrate the feasibility.

Panel discussion on the future of rifamycins for TB treatment in the face of resistance

P Phillips¹ ¹MRC CTU at UCL, London, UK. e-mail: patrick.phillips@ucl.ac.uk

This discussion will be moderated and guided by one of the session organizers who will both prepare questions and solicit questions from the audience. Questions will be addressed by the panel, comprising speakers and chairs. It will consider the larger question of whether efforts to preserve rifampicin are warranted in the face of growing resistance globally. Additional Topics will include the risks and opportunities afforded by rifamycins in TB treatment; discussion of higher doses of rifampicin than those presented in the talks, and if/how they should be further evaluated; and the prospects afforded by and lessons learned from clinical studies of the other rifamycins (rifapentine and rifabutin).

02. Pneumonia: supportive clinical management where there is no intensive care

How can risk stratification benefit children with pneumonia?

E McCollum^{1,2} ¹Johns Hopkins University School of Medicine, Pediatrics, Eudowood Division of Pediatric Respiratory Sciences, Dhaka, ²Johns Hopkins Bloomberg School of Public Health, Department of International Health, Dhaka, Bangladesh. e-mail: eric.d.mccollum@gmail.com

Mortality amongst children in low-income countries from pneumonia is high, and frequently complicated by hypoxemia, HIV, and malnutrition. Evidence of declining child pneumonia case fatality in countries such as Malawi are cause for hope, but mortality remains elevated and largely unchanged amongst high-risk groups. This talk discusses potentially innovative strategies for identifying high-risk patients and how such identification may feed into improved case management at referral health facilities and in rural communities of low-resource settings.

How can risk stratification benefit adult patients with pneumonia?

S Aston¹ ¹Royal Liverpool University Teaching Hospital, Tropical and Infectious Diseases Unit, Liverpool, UK. e-mail: stephen.aston@liverpool.ac.uk

The ability to accurately triage patients with pneumonia is key to improving the management of respiratory infection. Underestimating disease severity may lead to delays in starting appropriate treatment and increased mortality. By contrast, overestimating severity results in unnecessary hospitalisation and broad-spectrum antibiotic use. Several severity assessment tools (e.g. CURB65, IDSA/ATS criteria) have been developed to support clinicians to make early management decisions in pneumonia. In well-resourced settings, these tools have successfully been used to both identify patients at high risk of deterioration to target for early aggressive treatment and also to safely increase the proportion of low-risk patients managed in the community. However, all existing validated severity assessment tools have been derived in high-resource settings. When examined in low-resource settings - where patient populations are typically younger and have a different pattern of comorbid illness including high rates of HIV and TB - these tools have been found to perform poorly. This presentation will describe the process and challenge of developing accurate and practical severity assessment tools for use in low-resource settings. The performance of existing tools will be reviewed and then recent efforts to derive alternative tools better adapted for use in low-resource populations discussed. Finally, suggestions of how severity assessment tools may be incorporated into pneumonia management pathways and then evaluated will be presented.

Biomarkers of pneumonia: are new diagnostics on their way, or far away?

E Carrol¹ ¹University of Liverpool, Institute of Infection and Global Health, Liverpool, UK. e-mail: edcarrol@liverpool.ac.uk

Pneumonia is the major cause of death in children throughout the developing world especially in children under the age of 5 years. Most deaths attributable to acute respiratory infection are caused by pneumonia and bronchiolitis. The differentiation of bacterial and viral aetiologies is difficult on clinical grounds alone. Characterising biomarkers of severe bacterial infections could lead to rapid diagnostic tests with high discriminatory value. Individual biomarkers frequently fail to reach the threshold for clinical usefulness, but biomarker panels derived from disease related biological processes are likely to improve classification. This will help guide antibiotic management and decisions on referral to hospital.

03. Tackling second-hand smoking: a life course approach

Prevalence of second-hand smoke exposure during pregnancy: a secondary analysis of demographic and health surveys in 30 low- and middle-income countries

S Reece,¹ M Kanaan,¹ K Siddiqi¹ ¹University of York, York, UK. e-mail: sian.reece@york.ac.uk

Second-hand smoke (SHS) exposure during pregnancy is an important and avoidable risk factor for perinatal morbidity and mortality. Presently, there are no global estimates of the prevalence and attributable disease burden of SHS exposure in pregnancy. We used data from Demographic and Health Surveys to determine the magnitude of SHS exposure in pregnancy and its relation to maternal age, educational status, occupational status, wealth index, and characteristics of household smokers. Data was collected from 37,427 pregnant women from 30 low- and middle-income countries between 2008 and 2014. On average, 33% of pregnant women were exposed to SHS, reaching 72% in some countries, and 28% on a daily basis. The attributable risk of SHS exposure in pregnancy is likely to be higher than active smoking, where global prevalence is comparatively lower (2.6%) highlighting the importance of focused public health strategies to protect maternal and child health in this area.

Interventions to reduce home exposure to second hand smoke in pregnant women: findings from a systematic review and modified Delphi survey

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Background: Exposure to second-hand smoking (SHS) among non-smoking pregnant women is high in several low and middle income countries (LMIC) and is associated with adverse pregnancy and infant health outcomes. There is a paucity of research on use and effectiveness of behaviour change interventions (BCI) in SHS exposure reduction in LMICs. We plan to develop a comprehensive BCI package using available literature and expert consensus, and carry out a feasibility RCT in India and Bangladesh.

Methods: 1) Systematic review (SR): Two reviewers searched and extracted literature derived from eight databases for research published between 2000 and 2015 in 'English' language. Population: Pregnant woman assisting her spouse change smoking habit; Interventions: BCI used at home; Comparison: No intervention; Outcomes: Reduced SHS exposure at home or quitting

smoking or increased awareness. 2) Modified Delphi survey (MD): 30 experts were asked to rank a list of 21 BCIs in the order of priority based on their past research experience. Rankings from 17 experts across three rounds of consensus building were examined.

Results: Very stringent criteria yielded 327 citations of which 35 were reviewed and 6 were extracted. All the studies were health facility based and included 4 RCT and 2 before-and-after without control. Two studies used Health Belief Model and two used Trans-Theoretical Model. The common intervention used included information booklet, motivational interviews (telephone/in-person), health-professional advice, and videos. After the third round of modified Delphi, a modest but significant consensus among experts was achieved (Kendall's $w=0.61$; $P<0.001$). The highest-ranked interventions were cotinine feedback, providing information on the consequences of SHS, salience of consequences and barrier identification.

Conclusion: There is a dearth of literature and the quality of studies was moderate to low. The BCIs appear to be useful but limited to self-reported SHS reduction. Based on SR and modified Delphi survey findings we developed an intervention package entailing letter from unborn foetus to father, cotinine feedback, pictorial booklet and voice call to father. This BCI package is currently being piloted in India and Bangladesh. The findings will have important implications for scalability and sustainability of BCIs in reduction of SHS during pregnancy in LMIC.

Second-hand smoke exposure in children in a low-income countries with smoke free laws: a school-based survey in Bangladesh

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We report on second-hand smoke (SHS) exposure based on saliva cotinine levels among children in Bangladesh - a country with laws against smoking in public places. A survey of primary school children from two areas of Dhaka, was conducted in 2015. Participants completed a questionnaire and provided saliva samples for cotinine measurement to assess SHS exposure with a cut-off range of ≥ 0.1 ng/mL. 481 children aged 9-15 years were recruited from 12 schools. Of these, 479 saliva samples were found sufficient for cotinine testing, of which 95% (453/479) were positive for SHS exposure. Geometric mean cotinine was 0.36 (95%CI: 0.32-0.40); 43% (208/479) of children lived with at least one smoker in the household. Only 21% (100/479) reported complete smoking restrictions for residents and visitors; 87% (419/479) also reported being exposed to SHS in public spaces. Living with a smoker and number of tobacco selling shops in the neighbourhood had positive associations with SHS exposure. Despite having a ban on smoking in public places, SHS exposure among children in Bangladesh remains very high. There is an urgent need to reduce exposure to SHS in Bangladeshi children.

What can be done with schools to protect children from second-hand smoke exposure?

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We tested a school-based intervention designed to support families in implementing smoking restrictions at homes in Bangladesh in a two-arm pilot cluster randomised controlled-trial, conducted in 12 primary-schools and with 481 children. Outcomes included children's exposure to SHS measured by salivary cotinine concentration before-and-after the intervention. Our pilot trial findings suggest potential in the intervention to reduce children's exposure to SHS. There was a slight reduction in the mean cotinine concentration from 0.34 ng/mL (95%CI 0.30-0.39) at baseline to 0.30 ng/mL (95%CI 0.26-0.35) at follow-up in the intervention arm and from 0.38ng/mL (95%CI 0.33-0.43) to 0.36 ng/mL (95% 0.31-0.43) in the control arm. Compared to having partial or no restriction, complete smoking restriction at home was associated with a reduction in cotinine concentration. While the observed effect was in the right direction, the difference was not statistically significant as expected from a pilot trial. This warrants a definitive trial to study its effectiveness.

04. Active TB drug safety monitoring and management: a transformative approach to limit treatment-related patient harm

Limitations and problems of current MDR-TB treatment adverse event reporting

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Current MDR-TB treatment adverse event data from both randomized clinical trials and observational studies are sparse and challenging to work with. A recently completed systematic review of 74 studies reporting MDR-TB treatment outcomes published since January 2009 demonstrated that outcomes were much more completely and consistently reported than AE reporting - which was non-standardized, and incompletely reported in almost all of the publications. Problems reporting AEs included varying definitions, methods of ascertainment, and judgement of severity making pooling of results across studies difficult. In this session we will look at how uncertainties associated with poor quality or sparse data limits our understanding of toxicity and hence makes it very difficult to compare possible drugs to use when designing treatment regimens.

Reporting adverse events within the framework of aDSM: parameters and approaches

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The unsatisfactory treatment outcomes associated with current regimens for multidrug-resistant (MDR-TB) and extensively drug-resistant TB (XDR-TB) have motivated the introduction of new and repurposed medicines to treat patients with these conditions. This has at times happened ahead of the completion of trials. This trend poses some concern about the safety of medicines and novel regimens which have as yet only been used in limited contexts. The monitoring of adverse events (AEs) has not been one of the standard parameters which TB programme staff have monitored systematically when following up patients on TB treatment. This presentation will describe the rationale behind active TB drug-safety monitoring & management (aDSM) as a new programme activity, how it is being implemented, and the associated efforts to standardise the reporting of serious and other AEs in order to generate comparable country-level indicators and contribute to the global aDSM database.

Background information: <http://www.who.int/tb/areas-of-work/drug-resistant-tb/treatment/pharmacovigilance/en/>

Adverse events reporting for anti-tuberculosis medicines in the Philippines: current situation, experiences and lessons learnt

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Philippines is one of the 30 high TB burden countries in the world based on the listing of the World Health Organization. The initiative to address drug resistant TB started in the private sector in 1999 and was mainstreamed to the National Tuberculosis Control Program (NTP) in 2008. Treatment regimen is standardized and duration is for at least 18 months. Treatment success rate is low due to high loss to follow-up. Study was done and showed that the common causes of loss to follow-up were due to adverse drug reactions, need to work, personal challenges, geographic barriers and the duration of the standard regimen. With these challenges and the information of the successful use of the 9-month treatment regimen (9MTR) under operations research condition, the NTP decided to implement the 9MTR in 2015. With the use of the 9MTR and the use of bedaquiline, the NTP needs to have pharmacovigilance in place to ensure early detection and timely reporting of adverse events. In the Philippines, the Food and Drug Administration (FDA) is the agency that is mandated to implement the national Pharmacovigilance Program. Currently, the FDA utilizes only a spontaneous reporting system for most medicines. With the introduction of 9MTR and the use of bedaquiline, the NTP together with partners and the FDA is working towards an active drug

safety monitoring and management system. Currently paper based reporting system is used to report adverse events. To facilitate reporting and analysis of data, the NTP in collaboration with Systems for Improved Access to Pharmaceuticals and Services and the FDA is working on the use of Pharmacovigilance Monitoring System. Collaborative meetings were done to identify and harmonize the needs of the NTP and FDA. Reporting of adverse events for anti-TB drugs is challenging but based on the experience of NTP, it can be done with the coordination and cooperation of the different stakeholders. It is important that everybody in the system understands the significance of the initiative, roles and the responsibilities are well defined, and are informed and capable of the given tasks.

Improving TB patient safety and management: the Georgia experience

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Georgia was the first country to start MDR-TB patients on treatment through the USAID/Janssen bedaquiline donation program. In response to the WHO aDSM strategy, and to optimize safety of the patients on bedaquiline, Georgia established a system for collection, collation, and analysis of adverse event data in line with the core package requirements of aDSM. To enforce reporting using this system by TB facilities, a Ministerial order was issued mandating all serious adverse events for MDR-TB patients to be reported to the national center of TB and Lung Diseases. This session will present our experiences, results, and challenges implementing the system and will describe a web-based application to collect, analyze, report, and publish adverse event data captured while monitoring patients treated with new TB medicines in Georgia.

05. Addressing healthcare disruption and minimising drug resistance development among TB patients affected by conflict arising from armed resistance in Syria

Public health strategy for tuberculosis among Syrian refugees in Jordan

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This talk will outline the multipartner strategy developed with the goal 'To reduce susceptible and resistant tuberculosis transmission, morbidity, and mortality among Syrian refugees residing in Jordan'. The implementation and current statuses, including successes and setbacks, will be discussed.

The impact of the Syrian civil war on TB care delivery and the role of the international community

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The partisan nature of aid delivery has left an estimated 96% of civilians living in besieged areas without health assistance. The United Nations Office for the Coordination of Humanitarian Affairs has been unable to hold the government accountable for increasing attacks on health workers and hospitals, creating a dire health situation. The unavailability of drugs, constant migration of Syrians and breakdown of infrastructure, make a potential outbreak of tuberculosis and MDR-TB a serious threat.

Conflict and the interruption of TB treatment among Syrians

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The confluence of a decimated healthcare system, a thriving pharmaceutical industry brought to its knees, and the loss of healthcare workers have created an ideal environment for TB to spread, and the even uglier MDR-TB is likely gaining ground. The deliberate and accidental interference with the healthcare system has caused interruptions in the treatment regimens, which is a known risk factor for MDR-TB. As Syria empties of its people, they carry with them their TB across the region in what will likely be a serious setback in the fight against this disease.

06. Tuberculosis and diabetes collaborative activities in the context of the End TB Strategy and Sustainable Development Goals

Update on the global progress in implementing TB-diabetes collaborative activities

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The main objective of this presentation is to give further guidance to the global audience on how best to deliver integrated services for TB and Diabetes Mellitus (DM). The interaction between Diabetes Mellitus and tuberculosis (TB) has been known for many years now. In response to the growing global threat of TB and DM, the World Health Organization together with partners published the first global framework in 2011 following which countries started to translate the global recommendations into action. Based on the review of the global literature and limited country experiences, WHO issued a call to action in 2014. In this presentation, we will discuss global progress in terms of translating existing

global recommendations in to action and will suggest the way forward for further roll out at global level.

TB and diabetes: promising scalable models of TB and diabetes integration in resource-poor settings with dual burden. Lessons from World Diabetes Foundation (WDF)

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World Diabetes Foundation (WDF) has been in the forefront in an effort to generate evidence that aligns with the World Health Organization - collaborative framework for care and control of tuberculosis and diabetes with innovate and scalable models of TB and diabetes integration in resource-constrained settings with dual burden of TB and diabetes. Towards that end, WDF has piloted different models and also conducted a variety of operation research in the Americas, Africa, Latin America as Well as South East Asia. The objectives of this presentation is to share evidence of these existing and promising integration models and discuss steps that needs to be taken to move these models from pilot to scale.

Charting the course for integrative care: five years of TB-diabetes programme progress for the Pacific

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In 2014, 57% of adult Pacific Islanders with TB were also found to have diabetes. Six years ago, in parallel with the WHO Collaborative Framework for Care and Control of TB and Diabetes, seven Pacific nations adopted a common set of TB-DM Standards that provide guidance for bidirectional screening, a list of clinical reminders for TB clinicians, methods for optimizing glucose control during TB treatment, and suggestions for targeted latent TB screening as an opportunity for TB prevention. A recent meeting for Pacific TB Programs was held in conjunction with the 2015 APR Meeting in Sydney to mark our progress, identify best local practices, and chart a course for further implementation of TB and DM activities. This talk focuses on the pace and the progress for TB-DM implementation milestones in the Pacific. Challenges germane to all TB programs are highlighted.

Using TB and HIV platforms for prevention and control of diabetes mellitus: successful example from Ethiopia

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Background: Whether disease prevention and control platforms created under the TB and HIV programs could be used to address the growing threat of non-communicable diseases such as diabetes remains unanswered. Our objective was to demonstrate the feasibility of providing integrated clinical care for DM, TB, and HIV in general public hospitals in Ethiopia.

Methods: Between February-June 2015, trained health workers from TB, HIV, and DM clinics screened TB patients for HIV and DM; HIV patients for DM and TB; and DM patients for TB. A fasting plasma glucose (FPG) ≥ 126 mg/l or Random Plasma Glucose (RPG) ≥ 200 mg/dl was considered suggestive of DM. Patients in TB clinics received FPG tests because they take their anti-TB medications before taking breakfast while those in ART clinics received RPG tests. We used screening checklists which also served as data collection tools. Analyses included descriptive statistics of the baseline characteristics; calculating proportion of patients with diabetes, TB, or HIV among those screened; and binary logistic regression for adjusted analyses.

Results: Of 3439 study participants, 888 were from DM clinics, 439 from TB units, and 2, 112 were from HIV clinics. Six of the DM patients had TB of which five were already on treatment; the overall yield being 676 per 100 000 population. FPG was determined in 435 of the 439 TB patients. 141 (32.4%) TB patients had FPG ≥ 126 mg/dl, of which only five were known diabetic patients on follow up. Of 392 (89.5%) who knew their HIV status, 12.5% were co-infected with HIV. Symptomatic patients and those with risk score of 5 or more were about 2.8 times more likely to have abnormal blood glucose level. Of 2,072 HIV patients with random plasma glucose (RPG) determined, only 1.5% had RPG ≥ 200 mg/dl.

Conclusions: The yield of TB among DM patients was about three times the prevalence estimate for the general population. The integrated screening approach helped detect >90% of TB patients with abnormal blood glucose. Strengthening integrated screening practices can serve as entry point for addressing the growing threat of co-morbidities.

The TANDEM programme: understanding tuberculosis and diabetes through field studies and basic sciences

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TANDEM (Tuberculosis and Diabetes Mellitus), is a multidisciplinary EU-consortium which started its activities in 2013 (www.tandem-fp7.eu). TANDEM evaluates ways of screening TB patients for diabetes and vice versa in Romania, Peru, South Africa and Indonesia. Beyond screening, TANDEM studies clinical management of TB-DM patients, also looking at costs. In addition, consortium members in Germany, UK, South Africa and the Netherlands explore possible mechanisms of the associations between TB and diabetes. This is done at a genetic, transcriptomic and cellular level, using patient samples, in-vitro studies with macrophages and adipocytes, and animal experiments. This presentation will include some of the progress of TANDEM.

07. Introducing bedaquiline and delamanid for drug-resistant TB under routine programme conditions: preliminary results from the End TB initiative

Organising MDR-TB treatment with bedaquiline and delamanid: End TB in Armenia

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Armenia began providing MDR-TB treatment regimens that contain bedaquiline and/or delamanid to eligible patients under compassionate use in 2013 and in the context of the End TB initiative in April 2015. This End TB project is a collaboration between Médecins Sans Frontières and the Armenian Tuberculosis Control Centre and makes treatment with bedaquiline or delamanid available to MDR-TB patients in the country. We will report the number of patients, in civilian and prison populations, who initiated an MDR-TB regimen containing either bedaquiline or delamanid through May 2016 and the distribution of indications for receipt of these drugs. The frequency of two-month culture conversion and incidence of serious adverse events will be reported. We will discuss special challenges, innovations in treatment delivery including video DOT and decentralized treatment, and any advances and challenges arising from the introduction of the new drugs in the country.

Bedaquiline for the treatment of XDR-TB and pre-XDR-TB: End TB in Peru

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Peru began providing MDR-TB treatment regimens that contain bedaquiline and/or delamanid to eligible patients in February 2016. This End TB project is a collaboration between Socios En Salud and the National Health Strategy for Tuberculosis Prevention and Control of Peru. Patient eligibility is determined by a national committee of pulmonologists with expertise in treatment of DR-TB. Patient care is administered in homes or in a decentralized network of primary care facilities. We will report the number of patients who initiated an MDR-TB regimen containing either bedaquiline or delamanid through May 2016 and the distribution of indications for receipt of these drugs. The frequency of two-month culture conversion and incidence of serious adverse events will be reported. We will also describe the decision-making process, associated delays to treatment, and the transition from hospital to community-based care with continued intensive monitoring.

Bedaquiline and delamanid for MDR-TB in a setting of high HIV coinfection: End TB in Lesotho

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Lesotho began providing MDR-TB treatment regimens that contain bedaquiline and/or delamanid to eligible patients in November 2015. This End TB project is a collaboration between Partners In Health and the National Tuberculosis Program of Lesotho. HIV coinfection is present in approximately 75% of M/XDR-TB patients in Lesotho. We will report the number of patients who initiated an MDR-TB regimen containing either bedaquiline or delamanid through May 2016 and the distribution of indications for receipt of these drugs. The frequency of two-month culture conversion and incidence of serious adverse events will be reported. Results will be stratified by HIV serostatus. And, we will report the frequency of ART regimen adjustments among those coinfecting. We will discuss special challenges and any advantages arising from the management of HIV and treatment with the new drugs.

Bedaquiline and delamanid for MDR-TB in a setting of high HCV coinfection: End TB in Georgia

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Georgia began providing MDR-TB treatment regimens that contain bedaquiline and/or delamanid to eligible patients through compassionate use in 2012 and in the context of the End TB project in April 2015. This End TB project is a collaboration between Médecins Sans Frontières and the National Center for Tuberculosis

and Lung Diseases of Georgia. HCV coinfection is present in approximately 16% of M/XDR-TB patients in Georgia. We will report the number of patients, including those coinfecting with HCV, who initiated an MDR-TB regimen containing either bedaquiline or delamanid through May 2016 and the distribution of indications for receipt of these drugs. We will report on prison and civilian populations. The frequency of two-month culture conversion and incidence of serious adverse events will be reported. We will discuss special programmatic and clinical considerations for use of the new drugs in patients who are coinfecting with HCV.

Panel discussion: next steps for bedaquiline and delamanid for drug-resistant TB in End TB countries

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Session chairs will moderate and contribute to a panel discussion on themes emerging from the presentations, questions from the audience, as well as additional opportunities for innovation with the new drugs. This includes use of new drugs in pediatric populations as well as in combination, through compassionate use. And, panelists will discuss the End TB clinical trials, which will test all-oral shortened regimens containing at least one new drug in two different studies: one in patients with fluoroquinolone-susceptible MDR-TB and the second in patients with fluoroquinolone-resistant MDR-TB.

08. Tuberculosis in adolescents: confronting neglect, improving care

Global epidemiology of adolescent tuberculosis

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The epidemiology of tuberculosis changes significantly across the life-course. In endemic areas, TB incidence is lowest among children aged 5-9 years, and rises markedly through adolescence before stabilizing at a high peak. This suggests that early adolescence may be the key time-point for preventative interventions for TB within the lifetime of any given generation. With novel TB vaccines in development and significant advances in therapy for latent TB infection, intervening effectively with the current generation of adolescents could change the course of the global TB epidemic. In order to ascertain the potential impact of preventative interventions aimed at adolescents, it is necessary to understand the current epidemiological situation in this group. This talk will present estimates of the current incidence of TB among adolescents globally, and will also provide a detailed description of the epidemiology of TB among adolescents in a high TB transmission setting (South Africa's Western Cape Province).

Drug-resistant tuberculosis in adolescents and interventions to improve outcomes

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Treatment outcomes among adolescents with drug-resistant TB (DR-TB), with or without HIV-infection, are depressingly poor. The presentation will draw from Médecins Sans Frontières (MSF) data from various programmatic settings in Africa and Asia and from published literature, and will discuss patient outcomes and associated factors. We will present selected case studies to highlight challenges that adolescents face with treatment adherence but also with their life goals while on DR-TB treatment. Interventions to support adolescents to stay on treatment will also be presented and experiences from piloting such interventions will be discussed.

Adherence issues in adolescent TB and HIV treatment

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Outcomes among TB- and HIV-infected adolescents in high-prevalence, low-resource settings are consistently worse than those for adults. Both perinatally and behaviorally HIV-infected individuals are especially vulnerable to TB-related morbidity and mortality during their adolescent years. Diagnosis of adolescents is often delayed and adolescents face greater challenges maintaining adherence to their medications. This talk will explore some of the challenges to monitoring and supporting treatment adherence among adolescents with TB and HIV. We will discuss some of the developmental and behavioral characteristics of adolescents that should be recognized by practitioners in order to facilitate better treatment outcomes.

09. Screening for latent TB infection among migrants: from controversy to consensus?

Screening migrants for LTBI: review of the evidence on effectiveness and cost-effectiveness

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Immigrants contribute disproportionately to the numbers of notified cases and represent over a half of total notified cases in low incidence countries. The majority of TB episodes are the result of the reactivation of non-recent infection acquired in the home country. This is the rationale to promote a strategy for systematic testing and treatment of latent tuberculosis infection (LTBI). Over-

all, gaps of knowledge exist throughout the whole cascade of LTBI management. Testing requires selection of effective tests or combination of tests. The sequential use of tuberculin skin test (TST) followed by interferon release assays for those who are TST positive, followed by treatment of double positive individuals is proposed as the best choice in this population; however, cost-effectiveness and impact studies are limited. Moreover, the threshold of TB incidence in the home country above which the intervention is cost-effectiveness is still unknown. The development of a new generation of diagnostic tests that target incipient TB rather than persistent infection could be a game-changer in this area. Ensuring high treatment initiation and completion rates for LTBI regimens is an unsolved challenge. There is evidence that shortening the duration of treatment and reducing the rate of adverse events facilitates treatment completion. Isoniazid should be replaced by rifamycin-containing regimens. Ultra-short treatment based on daily rifapentine and isoniazid for one month is being investigated in persons living with HIV and could represent a significant advancement in this population. Overall, there are uncertainties on the impact of preventive therapy on TB incidence among asylum seekers at population level. Cost-effectiveness of the whole strategy has been investigated in several studies, but the large variability in assumptions prevent generalization of conclusions. Ultimately, LTBI management should be implemented as a public health strategy and supported by an efficient system for monitoring and evaluation. LTBI should become a notifiable condition and electronic-based tools for data collection and analysis should be established. The critical step to start scale up of implementation is the development of a strong advocacy campaign to generate political consensus and allow for the allocation of significant human and financial resources.

Guidance on programmatic management of latent TB infection: applicability for TB control in migrants

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Individuals with latent tuberculosis infection (LTBI) are a reservoir of *Mycobacterium tuberculosis* in a population and as long as this reservoir exists, elimination of tuberculosis (TB) disease will not be feasible. Management of LTBI requires the identification of infected individuals and adequate treatment of those identified. Migrants and other risk groups have been identified as relevant target groups for TB elimination activities. In some migrant groups a high proportion of individuals test positive for LTBI and migrant groups may thus benefit from programmatic management of LTBI. In 2013, the European Centre for Disease Prevention and

Control (ECDC) started the development of guidance on programmatic management of latent TB infection in the European Union and European Economic Area (EU/EEA) countries. In a first step, experts from the EU/EEA countries, candidate countries, and representatives from international and national organisations reached consensus on the components to be included in the guidance document. The main components identified were: diagnostic tests for LTBI; preventive treatment regimens; risk group specific interventions; and combining LTBI control with other health programmes. This step was followed by collection of the scientific evidence base using literature reviews, accompanied by mathematical modelling and cost-effectiveness studies. ECDC is also developing evidence-based guidance on the assessment and prevention of infectious diseases among newly arrived migrants in the EU/EEA. This guidance will include options for the prevention of HIV, hepatitis B and C, vaccine preventable diseases, and intestinal parasites, as well as options for the prevention of active TB and LTBI. In October 2016, the evidence base collection for both guidance documents will be far advanced or completed. This evidence will permit the assessment of options for programmatic management of LTBI in migrants and the assessment of whether there are gaps in the knowledge base.

Screening migrants for LTBI in Italy, Netherlands, Sweden and the UK: a comparative analysis

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This talk will present a comparison of policies, practices and M&E systems across four European countries, as part of a new EU project. This innovative project aims to pool data across countries to analyze LTBI screening coverage and results among migrants and the patient pathway from screening to diagnosis to treatment to treatment completion. It also includes policy analysis and qualitative studies to map interaction between health sector and migration authorities. The presentation will compare policies between countries and present early data on coverage and outcome of screening.

Intergovernmental Immigration and Refugee Health Working Group perspectives: pre-migration screening and the potential role of LTBI screening

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Health and migration authorities in low TB burden countries including Australia, the UK and the USA are

part of an Intergovernmental Immigrant and Refugee Health Working Group together with Canada and New Zealand. This group fosters intergovernmental collaboration and provides technical and programmatic guidance on pre-migration screening for refugees and immigrants. This joint presentation from representatives of Australia (Paul Douglas), the UK (Dominik Zenner), and the USA (Drew Posey) provides an analytic and comparative overview of pre-migration active and latent TB screening programmes of their countries including the range of different approaches and methods used and outline lessons learned, current initiatives and the way forward. Recent developments, such as the development of a common intergovernmental TB screening specification and other aspects such as role of migrant TB screening within their national TB strategy, evidence on priorities for TB screening and treatment among migrants, and monitoring and evaluation, will be covered. With the new emphasis from the World Health Organization through the End TB strategy, the importance of how these screening programs address the issue of latent TB and prevent future reactivation in low and medium incidence countries will be explored. The outcomes will demonstrate that premigration screening for active TB is successful in decreasing the incidence of TB in receiving countries but on its own will not meet the requirements to eliminate TB and must be used in conjunction with LTBI screening either before or after arrival.

10. Policy makers and partnerships: building the political will to end TB

Getting our attention: engaging policy makers on TB

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Building political support is key to ending TB, but it is hard to know where to start. The Rt Hon Nick Herbert, co-founder of the Global TB Caucus, will share how he became involved in the fight against TB and discuss opportunities to approach and engage busy policy makers.

Building champions in the Kenyan Parliament: how grassroots support led 100+ MPs to take action on TB

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On World TB Day 2015, MP Stephen Mule led a charge on the floor of the Kenyan Parliament that led to over 100 MPs to sign the Barcelona declaration, pledging to end TB in their lifetime. This presentation will explore how KANCO engaged MP Stephen Mule on TB issues, the tactics KANCO used to build broad bipartisan support, and how the collaboration between MPs and

civil society laid the foundation for over one hundred MPs to take action on an often forgotten disease.

How to engage your colleagues on TB: creating a national TB caucus in Georgia

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With the highest rate of drug-resistant TB in the world, the Eastern Europe and Central Asian region is a key battleground in the fight against TB. As a medical doctor, former National TB Program Manager, and current Member of Parliament, Dr. Khechinashvili used his political platform to create a national TB Caucus in Georgia's parliament. In this presentation, Dr. Khechinashvili will outline the steps taken to create a national caucus in the Georgian Parliament and identify opportunities for MPs to work together with civil society to create a TB-free world.

Building parliamentary support at a regional level: the Asia Pacific TB caucus

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Almost 6.2 million cases or two-thirds of the global TB burden are estimated to be in Asia, with 40% in just three countries: India, Indonesia, and China. The region is also the home of both established and fast growing economies, and countries that are transitioning out from donor support. In September 2015, members of the Global TB Caucus from India, Vietnam, the Philippines, Indonesia, Papua New Guinea, New Zealand and Australia formed the first parliamentary regional network under the Global TB Caucus; the Asia Pacific TB Caucus. The Caucus was formed with the intention of developing regional solutions to TB, which is a significant regional issue in the Asia Pacific. First, the Caucus focused on small, achievable asks that any individual anywhere could take. This gave a common objective for the TB community to support and helped to engage parliamentarians on the issue of TB, and provided a broad base of political support upon which the Asia Pacific TB Caucus has been built. There is a divide between political leaders and decision-makers, and those who know the disease best: those who work on TB, and those who have been affected by TB. By leveraging the engagement of colleagues in regional countries, the Caucus has been able to close that gap. Since the founding, Parliamentarians around the region have worked with each other to raise the attention given to TB, new comprehensive TB laws have been passed and are now being replicated, and donors Governments are now starting coordinate their TB investments. In addition to this, new regional and linguistic caucuses have been launched in the Americas, Africa, Europe, and Francophone regions. Each regional caucus has their own goals and achievements, but all are founded on one principle - Tuberculosis is in every country in the world, and we need the world to come together to address it. As the Caucus grows, it will focus

on strengthening the ties between political leaders and the TB community, and in doing so help unlock the resources and the policy changes needed to accelerate progress against the TB epidemic.

Engaging policymakers on TB in emergency settings: the case of Nepal

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While tuberculosis had always been a major challenge facing Nepal. Each year, approximately 45 000 people develop tuberculosis and around 35 000 get registered in NTP recording and reporting system. 10 000 new cases always missed out from being reported each year. Though NTP is planning to carry out a prevalence survey to unveil the real status of tuberculosis in the country, the current situation became more complicated in the wake of the devastating earthquakes of April 25th and May 12th 2015. The earthquakes affected thirty-one of the country's 75 districts. Approximately 9000 people lost their lives; more than half a million houses collapsed including government buildings, health facilities and prisons and almost 2.8 million people were displaced. The health and population sector was severely affected causing losses to health infrastructure and disruption of healthcare service delivery. As a result, the ability of health facilities to respond to health care needs had been affected and service delivery was disorganized. Consequently, vulnerable populations, including disaster victims, were further disadvantaged in accessing health services including DOTS in remote and affected areas. The disaster brought forward few challenges - maintenance of the disrupted services of national TB program (NTP) in the affected areas and engagement of policymakers in advocacy for both regulating existing services and high level support to NTP in the post disaster situation. Volunteers for Development Nepal (VFDN), a national NGO working in TB engaged along with other stakeholders in reorganizing the services and tracking of missed out patients in earthquakes hit districts as well as engaged with the members of parliament in foundation of Nepal TB Caucus to support and strengthen NTP initiatives at policy making level. As a result, 42 parliamentarians signed on the Barcelona Declaration and founded Nepal TB Caucus, giving TB a political status for the first time in Nepal. During emergency situation, VFDN finds partnership between civil society and policymakers would be essential in enhancing advocacy and maintaining disrupted services at different levels ultimately strengthening NTP in achieving the goal of Global TB to End TB by 2030 in the country and in the region.

11. Another transnational tobacco company in the making: the impact of the globalisation of the Chinese tobacco monopoly on tobacco control policies around the world

History, aims and aspirations of the Chinese monopoly

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The Chinese National Tobacco Corporation is the world's largest manufacturer of tobacco products in terms of revenues. This session puts spotlight on the history of the tobacco business monopoly in China. It also talks about the aims of the China Tobacco Industry to monopolise the world's tobacco trade, with special interest in LMICs.

China's monopoly role in tobacco agricultural sectors in Brazil

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China Tobacco is expanding its reach to Latin-American countries like Brazil in a big, aggressive way by forming joint ventures with the local tobacco exporters. These joint ventures have integrated countless tobacco farmers in the exploitative process to make more profits.

Impact on demand and supply side measures for tobacco control under expanding Chinese monopoly

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Before the United States and the European Union, China is the largest trading partner of Africa. Bilateral trade between China and Africa exceeded \$ 210 billion. Apart from the bilateral trade agreements China signed with many African countries, China is also recognized as a partner in development and cooperation for many of these countries. Major African countries have ratified the Framework Convention on Tobacco Control (FCTC). The presentation aims to provide examples from Africa based on the experiences faced due to the expanding strategies undertaken by China Tobacco Industry and its impact on farmers' livelihood and/or others intervention in tobacco control policy making by China Tobacco.

Impact on demand and supply side measures for tobacco control under expanding Chinese monopoly

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This session aims to provide examples from Latin America based on the experiences faced due to the expanding strategies undertaken by China Tobacco.

12. Reframing resistance: research and innovation to improve patient care and end drug-resistant TB

Progress and challenges on the road to a universal regimen

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Today's treatment for drug-resistant TB is toxic, expensive, and can be as long as 24 months or more with less than 50% of patients cured. Faster-acting and simplified all oral TB drug regimens containing three or four new drugs with no pre-existing resistance and less toxicity would be a game-changer. This presentation discusses the progress and challenges towards an enhanced TB drug regimen(s) that can address both drug-sensitive and drug-resistant disease, as well as the strategy over the next 5 years to drive the momentum in TB drug development toward the targets of the End TB Strategy with special focus on creating a more robust and sustainable pipeline of TB drugs.

Towards universal drug susceptibility testing: how could next generation sequencing support this goal

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Since 2002 there has been a gradual 1.3% per year decrease in the incidence of tuberculosis worldwide. Though this is an encouraging statistic it is being hampered by the growing incidence of drug resistant tuberculosis. One key to effectively controlling tuberculosis and the spread of multi-resistant strains is accurate information on drug resistance and susceptibility. Phenotypic solutions, although the current 'gold standard', are cumbersome, prone to error and time-consuming. Detection of resistance conferring mutations by molecular methods is an alternative which has been shown to work but it is only the beginning of a holistic solution for guiding patient treatment. With the introduction of new drug combinations and patients with potentially more complex resistance profiles, it is imperative to provide a more panoramic view of tuberculosis resistance patterns in order to allow for the implementation of correct, guided therapies and to fight further spreading of multi-resistant strains. An important set of genetic resistance

markers is already known, while at the same time a wealth of new genetic information is evolving with the identification of additional putative genes, intergenic non-coding regions and mutations associated with drug resistance. The rapid evolution of knowledge on the genetic foundations of tuberculosis drug resistance is indicating that sequencing will become the most appropriate and versatile technology platform to provide rapid, accurate and actionable results for treatment of this disease. Reductions in sequencing costs and operational complexity over the past years have brought NGS into use in clinical laboratories in high-income countries and expanded its utility as a public health and clinical tool. Harnessing NGS for LMICs will require a comprehensive analysis to understand the current country specific situations, potential end-to-end solutions and the right applications. Currently there are no 'plug-and-play' solutions for reference labs in the most affected countries. However, a program can be envisioned which will overcome the limitations and facilitate access to a comprehensive drug resistance genotyping solution for health authorities, tuberculosis treatment centres and patients in low- and middle-income countries.

Developing a vaccine to prevent all forms of TB

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Drug-resistance mechanisms are distinct from vaccine targets, and therefore an effective vaccine is expected to protect against all forms of TB, including drug-sensitive TB, multi-drug-resistant (MDR) and extensively drug-resistant (XDR) TB. A safe, effective vaccine will be crucial in stopping the spread of TB and drug-resistance. This presentation will discuss progress and challenges in developing new TB vaccines, and key areas of focus over the next 5 years toward the development of new, more effective TB vaccines as identified in the Global Plan to Stop TB 2016-2020, which include continuing to advance the clinical pipeline, enhancing knowledge through experimental medicine, increased emphasis on early-stage research, improving animal models, laying the foundation for adolescent and adult vaccination campaigns, and strengthening community engagement in vaccine R&D.

Intensified TB research is essential for re-centring care around the needs of TB patients

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Eleven years of data on TB R&D funding collected by Treatment Action Group demonstrates that TB R&D is gravely underfunded; a situation that imposes significant costs on health systems and carries direct consequences for patient-centered care. This presentation will demonstrate how intensified support for research and innovation is essential for improving patient-centered care in TB. The presentation will review efforts to ensure that

research reflects patient needs and priorities, and make the case that governments should see support for TB research as necessary for promoting dignity and meeting their obligations under international human rights law.

13. Monitoring progress towards the End TB Strategy target to eliminate catastrophic costs: findings from the first round of surveys

Findings from the first national TB patient cost survey in Ghana

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Even when tuberculosis (TB) care is free, impoverished patients, and their households, continue to incur unmanageable costs due to seeking and staying in care for the full duration of anti-tuberculosis treatment. In 2013, Ghana undertook a national TB prevalence survey which showed a generalised epidemic that is four times higher than previously estimated. This survey also highlighted barriers to accessing and adhering to TB care. Investigating and addressing these barriers, including direct non-medical costs (such as costs for travel and food during health seeking) is therefore imperative in order to inform the design of policies and interventions to ensure effective delivery of TB care, mitigate the economic impact of diagnosed TB for patients and their families, and ultimately contribute to reduction in burden of disease. This presentation will report on the process of establishing a nation-wide survey to assess the magnitude and main drivers of patient costs in Ghana. Preliminary findings will also be presented conditional on completion of data collection.

Findings from the first national TB patient cost survey in East Timor

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Tuberculosis (TB) remains an issue of public health importance in the Asia-Pacific region. Timor-Leste (South East Asia) reports an extremely high incidence rate of TB (498 per 100 000 population); much higher than the global rate, suggesting that further actions are needed to reduce the burden of TB. These actions should

address patient and household level issues which act as barriers to effective TB prevention and care, including the cost of health care seeking and TB care to patients. The proportion of households incurring catastrophic costs related to TB diagnosis and care is a new indicator in the End TB Strategy. It will be used to monitor progress towards TB elimination and therefore there is a need to establish baseline information on the economic burden of TB in each country. Here we report the initial results of a study that aims to estimate TB patient costs in Timor-Leste. A cross-sectional health-facility survey (with retrospective data collection and projections) was conducted in all but one health facilities that serve as TB DOTS centres. We aimed to recruit 445 TB patients (of all ages and all types of TB) sequentially as they attended the 16 participating DOTS centres, provided that they had undergone two weeks or more of TB treatment. One health care worker was trained in each facility to conduct face to face interviews with TB patients at the end of their routine clinic visits. Data collection was initiated in August and was planned to last approximately 2 months. We will calculate mean out-of-pocket medical and non-medical payments and indirect costs, before TB treatment starts and during TB treatment and will determine the proportion of TB patients who incur catastrophic costs and the amount of dissaving incurred. This research will be used to advocate for policies and interventions to: 1) minimise barriers in accessing and adhering to TB treatment and care, and 2) mitigate the economic impact of TB for patients and their families.

Findings from the 2016 national TB patient cost survey in Viet Nam

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This presentation will summarize findings from the first nationally representative survey of costs faced by TB patients and their households in Viet Nam (2016). The presentation will have 6 objectives: 1) To present rationale and backgrounds for this work in the context of Vietnam and the End TB strategy; 2) To present study objectives and methodology in line with WHO methodology; 3) To describe the adaptation of the survey instrument and electronic data collection tool experience; 4) To present the study process from fund raising to result dissemination; 5) To present preliminary results and findings; 6) To describe results dissemination process within and beyond the TB community.

Field testing the generic protocol for patient cost surveys: lessons learnt and way forward

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This presentation will summarize the emerging work to measure costs faced by TB patients and their households through periodic nationally-representative surveys in line with WHO methodology (2015). The presentation will have three objectives: 1) To present an outline of the generic protocol and instrument for measuring patient costs and the proportion experiencing catastrophic costs; 2) To share the experience from first implementing countries that have presented data in this symposium and from other countries that have completed or started surveys in 2016; 3) To provide advice to countries that are planning future surveys.

14. Enough is enough: time to end preventable mortality among people living with HIV

HIV-associated TB mortality: an irreversible truth?

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One third of all HIV-associated deaths were due to TB in 2014, and HIV autopsy studies show TB prevalence rates as high as 40%. Case fatality rates show PLHIV three times more likely to die than HIV-negative patients during TB treatment. Despite this, evidence has also shown that if given ART, HIV-positive TB patients can have outcomes comparable with HIV negative TB patients. This presentation will provide an overview of the evidence on mortality from HIV-associated TB and MDR-TB, highlighting the opportunities in the cascade of care through from early case detection to timely treatment to end preventable mortality.

The role of presumptive TB treatment for improving survival in severely ill patients with HIV

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Background: In 2007, World Health Organization (WHO) issued emergency recommendations on empiric treatment of sputum acid-fast bacillus smear-negative patients with possible tuberculosis (TB) in HIV-prevalent areas, and called for operational research to evaluate their effectiveness. We sought to determine if early, empiric TB treatment of possible TB patients with abnormal chest radiography or severe illness as suggested

by the 2007 WHO guidelines, is associated with improved survival.

Methods: We prospectively enrolled consecutive HIV-seropositive inpatients at Mulago Hospital in Kampala, Uganda, from 2007 to 2011 with cough for ≥ 2 weeks. We retrospectively examined the effect of empiric TB treatment before discharge on 8-week survival among those with and without a WHO-defined 'danger sign,' including fever $>39^{\circ}\text{C}$, tachycardia >120 beats per minute, or tachypnea >30 breaths per minute. We modeled the interaction between empiric TB treatment and danger signs, and their combined effect on 8-week survival, and adjusted for relevant covariates.

Results: Among 631 sputum smear-negative patients, 322 (51%) had danger signs. Cumulative 8-week survival of patients with danger signs was significantly higher with empiric TB treatment (80%) than without treatment (64%, $P < 0.001$). After adjusting for duration of cough and concurrent hypoxemia, patients with danger signs who received empiric TB treatment had a 44% reduction in 8-week mortality (risk ratio 0.54, 95% confidence interval: 0.32-0.91, $P = 0.020$).

Conclusions: Empiric TB treatment of HIV-seropositive, smear-negative, presumed pulmonary TB patients with 1 or more danger signs is associated with improved 8-week survival. Enhanced implementation of the 2007 WHO empiric treatment recommendations should be encouraged whenever and wherever rapid and highly sensitive diagnostic tests for TB are unavailable.

Strategies to end HIV-associated TB mortality are only as good as their implementation: lessons from Zimbabwe

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Zimbabwe has made significant progress in the response to HIV-associated TB, reducing TB-HIV mortality by nearly 80% from 2004 to 2014. Almost 90% of TB patients knew their HIV status in 2014 and over 85% of HIV-positive TB patients received ART. More than 85% of PLHIV registered in care were screened for TB and case notification was further bolstered by impressive scale-up of Xpert MTB/RIF resulting in more than 75% case detection of HIV-positive incident TB cases. This presentation will scrutinize the cascade of TB-HIV care delivered in Zimbabwe and highlight the challenges, successes and opportunities to increase access to quality delivery of the respective interventions for reducing TB incidence and ending TB mortality among people living with HIV.

WHO guidance: examining the latest policies and their potential impact on ending mortality from HIV-associated TB

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In 2016 WHO published the 2nd edition of the Consolidated Guidelines on the use of ART for treating and preventing HIV infection, the implementation of which could have a considerable impact on reducing HIV-associated TB. Recommendations incorporated within these guidelines were based on the latest evidence around ART for all people living with HIV at any CD4 cell count, optimal timing of ART for HIV-associated TB, presumptive TB treatment, and the latest algorithms to manage HIV-associated TB. This presentation will provide an overview of the new guidance and its potential for reducing mortality.

15. New approaches and innovations in TB vaccine research and development

Diversifying the TB vaccine portfolio

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Although the vaccine clinical pipeline is well-populated it lacks diversity in immunological approaches. An increasing number of potential strategies are being explored to broaden the immune responses generated by TB vaccine candidates, which currently have been selected, in part, based on their ability to elicit classical CD4⁺ and CD8⁺ T-cell responses. Novel immune responses currently being studied or under consideration include CD1-restricted responses to lipids and glycolipids; MHC-E-restricted responses, mucosal-associated invariant T-cells (MAITs), mucosal responses generated via aerosol vaccine vaccination; and tissue resident effector memory responses. This presentation will provide an overview of research being conducted in these areas, and opportunities for further exploration.

The role of a therapeutic vaccine in the fight against tuberculosis

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Treatment of Tuberculosis (TB) infection consists in administration of several antibiotics for an extended periods of time and is increasingly confronted with resistance. Although immune correlates of protection against *Mycobacterium tuberculosis* infection and/or its resolution are not yet fully elucidated, it is established that host's immune response including T-cell based responses plays a key role in the control and evolution of the infection. Therapeutic vaccines have emerged as a

component susceptible to potentiate antibiotic-based interventions in different ways: by either increasing efficacy and/or shortening treatment duration (in particular for MDR/XRD infections) as well as by preventing recurrence of infection or disease following antibiotic arrest. We will review efforts carried by the field in the development of such vaccines and how they could be positioned in clinical development.

Pulmonary mucosal vaccination and local immunity

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The most cost effective way to control the TB epidemic would be with an effective vaccination regimen. Preclinical animal data suggest the most effective way to deliver a TB vaccine is direct to the respiratory mucosa. We have completed two clinical trials evaluating the safety and immunogenicity of MVA85A, delivered by aerosol to healthy, BCG vaccinated adults. We are currently evaluating the safety and immunogenicity of delivering MVA85A by aerosol in healthy *Mycobacterium tuberculosis* infected subjects, and the safety and immunogenicity of BCG delivered by aerosol in BCG naïve healthy subjects. An update on ongoing trials will be presented.

Searching for correlates of immunity and protection

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Our understanding of how the human immune system protects against TB in incomplete, hampering rational approaches to develop new TB vaccine candidates. Because of these gaps in knowledge about TB and particularly about how humans respond to TB infection, efficacy trials of new TB vaccine candidates are large, long, and costly. This presentation will discuss the extensive research that is underway to identify correlates of risk of TB disease in persons with latent *M. tuberculosis* infection. These efforts have important implications for discovery of correlates of immunity and protection, which inform design and development of new vaccines and to accelerate the product development pathway.

16. Quinolones: from bench to bedside

Epidemiology of fluoroquinolone resistance in TB in 2016

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The fluoroquinolones have potent activity against *M. tuberculosis*, including multidrug resistant tuberculosis (MDR-TB). However, the effectiveness of this antibiotic

class is limited by drug resistance. Fluoroquinolone resistance is of increasing concern due to the widespread use of fluoroquinolones to treat other bacterial infections, including bacterial pneumonia and urinary tract infections. In some countries, fluoroquinolones are available over-the-counter. FQ resistance can be conferred by genetic mutations in their target, DNA gyrase. However, approximately 45% of phenotypically FQ-resistant *M. tuberculosis* isolates do not have the commonly-described resistance mutations in DNA gyrase. This could result in unacceptably low sensitivity of rapid molecular diagnostic tests, which currently utilize the common DNA gyrase resistance mutations. Recent work has demonstrated the importance of efflux pumps in FQ resistance in *M. tuberculosis*. The epidemiology of fluoroquinolone resistance in *M. tuberculosis* will be reviewed, including known resistance mutations and mechanisms, and their prevalence.

Diagnostic performances of existing molecular and phenotypic assays for the diagnosis of fluoroquinolone resistance

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As a consequence of the use of fluoroquinolones (FQ), resistance to FQ has emerged, leading to nearly untreatable, extensively drug-resistant tuberculosis. Conventional *M. tuberculosis* phenotypic susceptibility testing is cumbersome and takes several weeks. The recommended critical concentration, for FQ susceptibility testing, defined by WHO as the ability of the bacilli to grow on medium containing 2 or 4 mg/l ofloxacin, is to a large extent based on consensus rather than scientific evidence. Moreover, using a single breakpoint does not allow delineating the different levels of resistance, thus impeding therapeutic decision about whether maintaining or not FQ depending on the resistance level. Therefore, molecular assays allowing rapid detection of resistance to antituberculosis agents are of major interest in routine practice. We will review the advantages and drawbacks of the available phenotypic and genotypic methods for FQ resistance in *M. tuberculosis*, in regard with the laboratory capacities.

Can fluoroquinolones be used for the treatment of XDR-TB? Lessons from animal studies

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Fluoroquinolones (FQ) are the corner stone of multidrug resistant tuberculosis (MDR TB) treatment. As a consequence, FQ resistance is the major element of the poor prognosis of XDR-TB defined as MDR-TB with additional FQ and aminoglycoside resistance. Although cross resistance between the members of the family is the rule for FQ, in vitro data have shown that some FQ-resistant strains remain susceptible to the most active FQ,

such as moxifloxacin (MXF), gatifloxacin or levofloxacin. These data were confirmed by murine studies showing that MXF has residual activity which can improve the sterilizing activity of a second-line drug combination. Moreover, the benefit of including FQ in a regimen used to treat TB patients infected by a FQ-resistant strain has been confirmed clinically. These data regarding the usefulness of FQ to treat XDR-TB will be reviewed, with a highlight on the strains for which FQ can be used.

Can fluoroquinolones be used for the treatment of XDR-TB? Lessons from human studies

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Background: XDR-TB is by definition resistant to fluoroquinolones. However, there is a large difference of power, with minimal inhibitory concentrations (MICs) for susceptible bacilli ranging from 2.0 for ofloxacin to 0.25 mg/L for gati- and moxifloxacin. The mutations causing fluoroquinolone resistance bring along a modest rise of the MIC, and only some render the bacilli resistant also to the most powerful fluoroquinolones.

Methods: in vitro experiments showed that killing of TB bacilli happens at the usual fluoroquinolone dose, but resistant mutants survive, except at double dose moxifloxacin. The group of Veziris in Paris was then able to show the same in mice, but only for bacilli with moxifloxacin MIC not higher than 2 µg/ml. We analyzed the outcome of a cohort of over 500 patients MDR-TB patients treated with the Bangladesh short regimen, a high-dose gatifloxacin-based standardized regimen, and checked their strains by MIC and DNA sequencing.

Results: There was no difference in survival (about 90%) between the fluoroquinolone susceptible versus a low-resistant subset with gatifloxacin MIC below 2. However, survival dropped to 51% for patients from another subset with MIC ≥ 2. Almost all these fluoroquinolone-resistant cases had bacilli sensitive to kanamycin, and of two XDR treated with the unmodified high-dose gatifloxacin regimen, both with MIC=2, one was cured. We found a clear correlation between mutation and MIC. Only mutations in codon 94 of *gyrA*, with exception of 94Ala, brought along high-level fluoroquinolone resistance. Also double mutations and rarely others showed high-level resistance.

Discussion: Low- and moderate level fluoroquinolone resistance did not seem to adversely affect the outcome of the Bangladesh regimen, using high-dose gatifloxacin as the core drug. Specific gyrase gene mutations confer high resistance with high risk for bad outcome, in pre-XDR as well as XDR. The Hain GenoType second-line LPA allows to identify most of these high-level resistance mutations, and could be a rapid and more feasible alternative than MICs in endemic countries. Replacing

the fluoroquinolone by one of the new drugs in the same background regimen may then restore its effectiveness.

17. Driving real-time access to diagnostic data through connected diagnostics

Analysis of the essential elements of connectivity solutions

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Diagnostics connectivity solutions have been introduced around the world as tools with the potential to improve quality of testing, facilitate supply management, reduce delay in starting treatment, strengthen clinical management, and facilitate surveillance. However the introduction of technology alone does not guarantee positive health system impact; consideration also needs to be given to support, training, utilization, monitoring and evaluation amongst others, in order to allow for the full potential of connectivity solutions to be attained.

Integrity of connectivity to the success of the larger investment in diagnostics

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How connectivity solutions are integral to the success of the larger investment in diagnostics, and how they should be truly integrated across the entire diagnostic landscape (TB, HIV, etc.) to better ensure local ownership towards sustainability.

On the ground experiences and challenges of a connected diagnostics intervention

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Impact, challenges and lessons learnt from the introduction of GX Alert in Nigeria.

Background/Rationale: With the adoption of GeneXpert machine by WHO in 2010; Nigeria commenced the rollout plan in 2011 with the aim of improving TB diagnosis among PLHIV and DRTB among presumptive DR-TB patients. Originally, GeneXpert was meant to ensure early diagnosis (2 h turnaround time [TAT] within the machine); unfortunately, the programmatic TAT was more than 2 weeks (i.e. sample collection, referral, and result retrieval to patients). GxAlert was primarily incorporated into the GeneXpert machine to ensure timely result reporting to both patients and healthcare workers (HCWs); fortunately, it turned out to provide more services (laboratory management tool).

Objectives: To describe the learning process of the different roles and facets of GxAlert over time.

Methodology: Cooperative linkage between Cepheid and GxAlert providers, multiple in-country stakeholders meeting to review of reporting tools; identification of additional potentials of GxAlert technology; piloting and roll-out of additional platforms for use of GxAlert; capacity building at various levels; identification and modification of internet providers; Supervision, Monitoring & Evaluation and linkage with NTP surveillance system.

Results: Currently, 185 GeneXpert machines are connected to GxAlert. And the following services are provided: Immediate feedback of test results to patients, health care providers and TB program staff; Status of cartridges utilization and stock; Maintenance related issues of the machines; Expected expiration of warranty; and overall routine data reporting on performance of the machines (total test, MTB detected, RIF resistance, errors and invalid results).

Challenges: Weak internet connectivity; difficulty in linking other electronic systems (DHIS and E-TB manager); unavailability of unique identifiers for patients with a double counting of patients with repeated test; quality primary data (correctness and completeness of sample request form); and low utilization of the platform for decision-making at various levels.

Conclusion: Connectivity or equipment is not a replacement for quality laboratory personnel, but a complementary tool and GxAlert is a laboratory management tool.

Experience piloting RemoteXpert and planned integration with Nikshay

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Impact, challenges and lessons learnt from the introduction of a connectivity solution in India.

The impact of connectivity solutions on key programmatic and laboratory indicators

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The investment, implementation and utilization of connectivity solutions are increasing but what impact is being seen on key programmatic and laboratory indicators? What are the other indicators of success and how do we measure them?

18. Ending TB transmission, stepping up TB infection control: lessons learnt, opportunities in sight

Namibia's experience in implementing TB infection control: lessons learned

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Background: Namibia is sparsely populated, with a population of 2.3 million. The country had a high estimated incidence of tuberculosis (TB) of 561/100 000 and a case notification rate for new and relapse cases of 472/100 000 in 2014. About 44% of the cases reported in 2014 were new smear-positive cases; while 44% of TB patients were HIV-positive. 143 cases of MDR-TB (including 6 XDR-TB cases) and an additional 206 cases of rifampicin resistance were notified in 2014. TB patients are primarily managed as out-patients; admission is usually for medical indications. Anecdotal reports suggest significantly higher TB rates among health workers than the general population.

Interventions: A package of tuberculosis infection control (TBIC) measures was put in place based on the national strategic plan, including development (2009) and revision (2014) of the National Guidelines for TBIC. Implementation was streamlined into the overall infection control programmes at national (coordinated by a national TBIC office and a resident architect) and implementation level. Infection Control Committees coordinated development and facility-level implementation of TBIC plans through TBIC focal persons. Training was cascaded from national to district and to facility levels over a period of 2 years. Key indicators focus on the number of staff trained and TB screening and diagnosis among health workers. TBIC focused health facility assessments were conducted; followed by targeted engineering modifications (UVGI and directional fans) and renovations (windows and outdoor waiting areas) which prioritised DR-TB and HIV treatment sites, and subsequently primary health care facilities. These were primarily funded by PEPFAR and Global Fund. N95 respirators were introduced, supported by a respirator fit testing programme.

Lessons learnt: Implementation of TBIC requires sustained advocacy and reinforcement. Numerous 'bad' TBIC practices recurred where supervision was inconsistent. Direct verifiable indicators for TBIC are lacking, making it difficult to demonstrate short-term benefits. There has been variable uptake of TB screening by health workers, with some opting for private medical care. Long-term measures should include infection control considerations in ministerial health facility standards and norms. A dedicated focal person and comprehensive guidelines were crucial to sustained implementation. Flexible partner funding facilitated timely minor facility modifications.

Early impact evaluation of the tuberculosis infection control training centre: Tajikistan, 2014-2015

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Background: The Central Asia Republics (CAR) region is composed of five independent countries that were once incorporated in the former Soviet Union; Kazakhstan, Kyrgyzstan, Tajikistan, Turkmenistan, and Uzbekistan. Tuberculosis (TB) prevalence for this region is just under 200 cases per 100 000, with a range of 122 cases (Uzbekistan) to 196 (Kyrgyzstan) cases per 100 000. Transmission of tuberculosis in health care facilities has contributed to the TB burden within the CAR region; research has demonstrated occupational risk of TB for health care workers (HCWs), particularly in facilities where TB infection control (TB IC) practices are absent. To develop human resources to strengthen TB IC practices within the region, Project Hope and USAID teamed with the Ministry of Health and Social Protection of Population Republic of Tajikistan to establish a TB IC training center for HCWs.

Methods: We assessed the initial impact of the TB IC training by conducting cross-sectional post-training evaluation interviews with an average of 10 months between training completion and evaluation. The eligible study population included all 89 HCWs who had attended at least one training during April 2014 - February 2015 at the TB IC training center at Machiton.

Results: Eighty-four of 89 (94%) participants completed the interview; reporting high levels of training satisfaction. Eighty (95%) participants reported meeting with workplace leadership to discuss the training. Of those, 69 (85%) reported discussing needed changes in their workplace to meet TB IC standards. Participant self-reported changes in TB IC practices at work facilities post-training included: creating TB IC committees, designating a TB IC focal person, TB IC planning, policies to separate infectious patients in waiting rooms, provision of masks for infectious patients, cough etiquette policies, improved glove availability, hand hygiene programs, and TB IC posters in waiting rooms.

Conclusions: High participation and satisfaction rates with encouraging TB IC knowledge retention scores (compared to pre-training scores) demonstrate potential for these trainings in improving TB IC practices in the CAR region. Future trainings may be tailored to specific audiences to impact administration, budgeting, and facilities management of TB IC practices.

Occupational risk factors for TB among health workers: policies and practices

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Health care workers have a two to three-fold increased risk of developing TB than the general population even in settings with high burden of TB in the community. This talk will address the international occupational health and infection control policies related to the health and safety of health care workers with a particular focus on health care workers in low-resourced settings.

Progress in the sustainable application of highly effective upper room germicidal ultraviolet air disinfection

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Natural ventilation is an essential environmental TB transmission control intervention, but by definition, it is not applicable in all locations day and night, or season to season. The most cost-effective supplement or substitute for natural ventilation is upper room germicidal UV air disinfection (GUV) with air mixing. New research has demonstrated high levels of efficacy under hospital conditions and have resulting in practical guidelines. Remaining barriers to wider, sustainable implementation are being addressed, including sound business models for commercial comprehensive GUV design, installation, commissioning, and maintenance services. Other advances include the emergence of LED UV technology that can run on batteries and solar power. Initiatives in India, China, Ethiopia, South Africa, and Myanmar will be presented.

SYMPOSIA: FRIDAY 28 OCTOBER 2016

19. Implementing pillar three of the WHO's End TB Strategy at the country level: lessons learned from path-finding countries

Implementing Pillar 3 of WHO's End TB Strategy at country level

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While the past decade has seen significant reduction in Tuberculosis (TB) prevalence and mortality, TB still kills 1.5 million people annually and is now the leading infectious cause of death in the world. To fight this epidemic, the World Health Organization (WHO) has developed the End TB Strategy, which aims to reduce TB deaths by 95%, to cut new cases by 90%, and to ensure that no family is burdened with catastrophic expenses due to TB care. 'Intensified research and innovation' has been identified as one of the three essential pillars to end the global TB epidemic. Research on improved implementation of existing tools as well as development of new technologies and interventions are essential aspects of this pillar. As part of Pillar 3 of the End TB strategy a Global Action Framework for TB Research (GAF) has been developed by WHO to foster high-quality national TB research to end domestic TB epidemics. A key output at country level is the development of country-specific TB research plans based on gaps identified through situational assessment of the TB epidemic, National TB Control Programme (NTP) performance, and health system assessment in the context of TB. In view of the substantial heterogeneity in risk for TB infection among different sub-populations, we are piloting the utility of mathematical modelling to assist countries in selecting research priorities that may achieve maximum epidemiologic impact on key high risk populations in a cost-effective way. To achieve the goals and milestones of the End TB Strategy, global efforts must be complemented by country efforts. In the presentations that follow, case studies of national TB research networks, and mathematical modelling applications for research prioritization are used to demonstrate novel, evidence based methods for research prioritization. These presentations also demonstrate how country specific research prioritization and capacity building is critical in impacting local TB epidemiology.

The role of Ethiopia's TB research network (TRAC) in driving the agenda for TB research

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This presentation will outline Ethiopia's efforts and achievements in using its multidisciplinary and multi-stakeholder TB research network to develop and implement a national TB research agenda.

Using current country level socio-economic data to define high-risk groups for targeting interventions: the S-Protect project

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Since 2003 Brazil has run the Bolsa Familia Programme (BFP), the national conditional cash transfer program to poor citizens. With 13 million beneficiary families (nearly 50 million people) around the country, BFP is today the largest conditional cash transfer programme in the world. BFP targets extremely poor households earning between US\$35-70 per person per month. Depending on the household composition, the monthly cash benefits range from US\$18 to a maximum of US\$175 and are given under three conditions: 1. attendance at prenatal and postnatal monitoring sessions; 2. access to nutrition and vaccination monitoring for patients' children aged 0-7 years; 3. school attendance. Besides that, the Sistema de Informação de Agravos de Notificação (Notifiable Disease Surveillance System database; SINAN) offers detailed information on patients diagnosed with incident TB and is considered a proxy of disease incidence. To achieve targets of the WHO End TB strategy, there is a need for intensified research to deliver new tools and strategies to combat the disease, linked with relevant epidemiological indicators and outcomes. The Technical Advisory Group (TAG) for TB Research Investment Case from WHO and the S-PROTECT initiative are developing methods together to find key elements to improve risk group interventions and inform research to achieve End TB targets. In Brazil, recent linkage between SINAN and Bolsa Familia programme data suggest that only 25% of TB patients are currently enrolled into Bolsa Familia Programme and that among them about 20% do not receive cash transfers while on treatment and therefore do not truly benefit from the social protection efforts of the programme (Torrens et al, 2016). It has been speculated that the low proportion of TB patients currently enrolled within BFP may be due to the high specificity, but low sensitivity of the deterministic approach taken for the data linkage. Since 2015 the National TB program now includes in the notification form the variable 'bolsa familia beneficiary'. We are analyzing TB and socioeconomic data from 31,402 patients now available in SINAN to improve comprehension on social protection

in the outcome of tuberculosis treatment and development of targeted models for TB decision-making.

Modelling for evidence: defining country-derived research questions and answers

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This talk will highlight the development of a core relationship between researchers, policymakers, and modellers in using country level data to answer NTP derived policy questions while creating a collaborative research community (TB Think Tank).

20. Challenging tuberculosis in urban settings and big cities in comprehensive TB control programmes

Strengthening TB service provision through urban DOTS in Kampala, Uganda

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Uganda's capital city, Kampala, population 1.5 million, contributes 20% of the 47,000 TB cases notified annually. Kampala has had low TB performance due to health system constraints, mobile population, limited access to TB treatment, private sector engagement and weak social support system in Kampala. In 2013 The National Tuberculosis and Leprosy Programme and Kampala Capital City Authority with support from the USAID-funded TRACK TB project implemented an Urban DOTS model including a city TB coordination mechanism, functional multi-disciplinary TB care teams, increased TB diagnostic and treatment facilities; strengthened M&E system; and engaged community volunteers to implement DOTS, patient support and strengthen facility-community linkages. DOT improved from 6% in 2013 to 89% in 2015; patient loss-to-follow-up reduced from 26% in 2013 to 3% in 2015; cure rate improved from 24% in 2013 to 78% in 2015; TSR improved from 16% in 2007 to 89% in 2015.

Addressing the TB control issue in fragile states: urban DOTS experience in Kabul, Afghanistan

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Background: Kabul suffers from population density and overcrowding and poor health infrastructure and TB indicators compared to national levels. Before 2009, case

notification and treatment success rates (TSR) were 26% and 49%, respectively.

Intervention: The National Tuberculosis Programme (NTP) with support from USAID-funded TBCAP, TBCARE I, and Challenge TB projects, implemented the following interventions: an Urban DOTS strategic plan for Kabul (2010- 2014); strengthening partnerships and coordination among NTP, public, and private health facilities; engaging public and private health facilities to provide TB services; raising community awareness about TB detection, diagnosis, treatment, and prevention; implementing SOPs for case detection/treatment; addressing vulnerable populations; promoting contact investigation; and implementing supportive supervision and monitoring. In 2016, the NTP and Challenge TB technical teams conducted an assessment to evaluate the role of Urban DOTS on TB case notification and treatment in Kabul. The assessment team reviewed TB data from the intervention period (2010-2016) and compared it with national TB surveillance data prior to 2009.

Results: DOTS coverage reached 81% in 2016, from 21% in 2009. Also in 2015, 17,525 presumptive TB cases were identified and examined; 1,449 (8%) were diagnosed as bacteriologically confirmed and 5,449 as all forms of TB. Among 5,449 TB cases, 612 were detected by the private health sector (11%), reflecting significant improvement in TB case notification. All forms of TB case notification increased by 182%, newly bacteriologically confirmed TB cases increased by 78%, conversion rate improved by 26%, and the TB patient treatment success rate improved by 24% to reach 73%.

Conclusion: Urban DOTS contributed to significant improvements in Kabul's TB case notification rate, sputum smear conversion rate, and treatment success rate. We recommend Urban DOTS be scaled up in Kabul, other cities in Afghanistan, and similar settings.

TB in urban settings and big cities in Latin America: general overview

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Latin America (LA) is one of the most urbanized regions in the world, with 80% of its population living in cities. In LA cities it is estimated that over 100 million people live in slums, one in four inhabitants lives in poverty, without universal access to basic services such as water and sanitation, in poor housing conditions and with limited access to health care. All these create vulnerability for tuberculosis (TB). The TB epidemic is declining in LA reaching 42 cases per 100 000 inhabitants, but each year the national TB programs (NTP) fail to diagnose more than 60 000 cases. In order to overcome this gap, the NTPs should focus their actions towards TB vulnerable populations, especially those living in slums of large cities. After analyzing where the missing cases are and reviewing the burden of TB in cities, PAHO/

WHO developed an initiative to address TB control in this context detailed in the document 'Framework for Tuberculosis Control in Large Cities of Latin America and the Caribbean'. It has the following components: 1) Strengthen political commitment at the national and local levels, and coordinate the different health authorities; 2) Conduct epidemiological mapping of the TB situation in cities and identify at-risk populations; 3) Survey and map the health system and existing health-care providers; 4) Adapt health care to the needs of the populations at risk; 5) Take an interprogrammatic approach to TB control to guarantee comprehensive patient care; 6) Take an intersectoral approach to TB control and include TB in social protection programs; 7) Promote civil society engagement in TB prevention and control activities and 8) Establish a routine monitoring and evaluation system. This framework has been implemented in more than 8 cities in LA. The implementation process includes a situation analysis followed by the components of the framework and an action plan adapting TB control in these contexts.

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Challenges to improve TB case detection and quality of care in big cities in Latin America: experience of Lima and Callao, Peru

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Lima the capital city has an estimated population of 10 million inhabitants. Peru has a large TB and MDR-TB epidemic, concentrated in Lima and Callao, with about 31,000 TB patients notified nationwide-60% of TB and 79% of MDR-TB patients whom live in the capital city. Following the WHO/PAHO framework, the Peruvian MOH since 2012 has implemented interventions focused in hot spots and slum populations in Lima and Callao: epidemiological mapping of TB focusing on two high burden TB and MDR-TB districts; mapping of both public and private health facilities, including informal providers; a baseline assessment of public hospitals; study of socio-economic characteristics of the population in high burden districts. Presentation of these interventions will focus on increased TB case detection; improved access to rapid tests for DR TB; reduction of default rate of TB and MDR-TB patients; improving the TSR; and reducing TB and MDR-TB incidence.

The perfect storm: the convergence of clinical and social complexity in London, UK

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Tuberculosis (TB) in London mainly affects those born in countries of high incidence or those with social risk factors (including homelessness, problem drug or alcohol use and imprisonment). We studied a cohort of 12 908 adult London TB patients, diagnosed 2009 to 2012, using surveillance data and used multivariable logistic regression to examine the effect of social risk factors on infectiousness (sputum smear positive pulmonary disease), isoniazid resistance, multidrug resistance (MDR-TB), non-adherence to treatment and poor treatment outcomes (failure to complete an un-interrupted course of treatment). The convergence of clinical and social complexity demands an integrated model of care with sustained public health and social protection interventions to improve clinical outcomes, control transmission and prevent further emergence of multidrug resistant disease.

21. MDR-TB and migration: from infection fundamentals to programme innovations

Overview of MDR-TB in migrants: epidemiology, increased risks and clinical specific issues to addressing MDR-TB in mobile populations

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This talk will provide an overview of the latest scientific evidence on MDR-TB overall, with a focus on MDR-TB and migration issues to achieve prevention, treatment and control.

Accessing MDR-TB treatment: labor migration in Tajikistan, and the journey of a MDR-TB patient crossing borders to access better care

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The Republic of Tajikistan included to the WHO list of the 27 countries with the high burden of MDR-TB.¹ The official statistics show that the proportion of returned Tajik migrant workers among registered new TB cases has increased from 13.5% in 2011 to 19.7% in 2015. The growing number of MDR-TB cases among Tajik migrants is also alarming: from 110 MDR-TB cases among Tajik migrants in 2013 to 154 cases in 2014. TB-HIV cases among Tajik migrants raised from 8 persons in

2013 to 21 persons in 2014. IOM conducts surveys, regular literature review, interviews with the national and international experts, returned migrant workers to develop evidence based interventions among migrant workers in Tajikistan. Studies among Tajik migrant workers demonstrated that being the main 'breadwinners' of their families migrants have poor health seeking behaviors due to fear of retrenchment, despite health deterioration. Analysis of the factors that influence to delay for TB treatment in Tajikistan showed that patients who develop TB while working abroad have the longest health system delays. High cost and fear of deportation were named as main barriers to the access to health care in the countries of destination. Moreover diagnostic and treatment of the communicable diseases such as TB are not covered by the insurance in the host countries. In addition to institutional barriers gender differences also contribute to the health seeking behavior of migrant workers. Male migrants are less likely to contact doctors, they approach health providers only in life-threatening situations at the end stages of disease progression. To address TB issues among migrants IOM in Tajikistan jointly with the health authorities piloted a number of the innovative approaches to improve migrant's access to TB diagnostic and treatment: community engagement, multisectoral approach, providing services on treatment adherence, offering food packages, income generation for livelihood, for developing small business, empowering TB cured migrants by involving them to advocacy campaign for reducing stigma and discrimination toward TB patients, engaging diaspora and promoting cross border TB prevention activities among migrants.

Reference

[1] http://who.int/tb/publications/global_report/high_tb_burden/countrylists2016-2020.pdf

Accessing MDR-TB treatment: decentralised management, challenges and opportunities in ensuring timely diagnosis, continuity of care and monitoring of MDR-TB treatment in India

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In many countries, MDR-TB treatment facilities are limited and centralized, forcing patients to shift residences to avail treatment. The National TB Program in India has addressed this issue by decentralizing the MDR-TB treatment and integrating it with the regular first line treatment. During the initial years of PMDT, patients were required to travel far from home to the MDR-TB centres for pre-treatment evaluation and initiation of treatment. Today patients can be diagnosed and receive treatment locally. The MDR-TB drugs are available at all the peripheral centres and are administered at the peripheral health facilities (usually for the injectable phase) and also by trained community DOT providers making it convenient for the patients.

Increased risk for MDR-TB for labour migrants in Southern Africa, especially miners

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Migration, both in the informal sector and among certain occupations like mining, is a key factor to consider in innovative program approaches to MDR-TB prevention, treatment and control. The National TB Program Manager of Lesotho will share her experience in dealing and managing MDR-TB cases in Lesotho and the Region as a whole. The presentation will be a shared presentation by the Lesotho NTP and the National TB Control Managers Working Group for Southern Africa.

MDR-TB in migrants: a gender and children perspective

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Dealing with deep-seated socio-cultural issues is key to ending epidemics. The gendered dimensions of TB are stark. Globally, of the estimated 9 million people who developed TB in 2013, over 60 per cent were men, and nearly two thirds of the estimated 1.5 million TB deaths in 2013 were among men. At the same time, TB kills more women globally than any other single infectious disease, and more women die annually of TB than of all causes of maternal mortality combined. Women who are co-infected with TB and HIV are significantly more likely to die of TB than co-infected men. The Global Fund Strategic Framework 2017–2022 emphasizes the importance of addressing the age and gender related disparities in accessing services that often drive epidemics, and the importance of scaling-up programs for women and girls. This talk will provide updated insights into MDR-TB programming principles and approaches for migration from a gender perspective.

22. New approaches to MDR-TB treatment in children: from research to evidence-based implementation

Scientific and clinical rationale for the substitution of a novel TB drug for the injectable agents in MDR-TB treatment regimens in children

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Background: Although treatment outcomes in children with MDR-TB are generally good, the injectable agents are poorly tolerated and often result in permanent sensorineural hearing loss, which affects children's developing brains more than it would adults. Novel TB drugs are now becoming available and have the potential to greatly improve MDR-TB treatment in children. This

presentation will provide a scientific and clinical rationale for substituting the novel nitro-imidazole delamanid (DLM) for the injectable agents in MDR-TB treatment regimens in children. This will be based on a recent review of the evidence on DLM, the injectables, and other agents for the treatment of MDR-TB, while crafting the protocol.

Methods: The IMPAACT 2005 study is a planned Phase I/II open-label, single-arm, multisite study to characterize the safety, tolerability and pharmacokinetics (PK) of DLM in children (aged 0 months to < 18 years) with MDR-TB, either with HIV co-infection on antiretroviral therapy (ART) or without HIV co-infection, and to define the potential application of DLM as a modality for the treatment of pediatric MDR-TB. Study drug will be given concomitantly with OBR for MDR-TB; where possible and where compatible with local guidelines and susceptibility pattern, children will receive an injectable-sparing OBR for MDR-TB that includes four active drugs.

Results: The study is, at the time of abstract submission, still going through regulatory proceedings and has not yet begun enrolling.

Conclusions: Delamanid is a promising new option for the treatment of MDR-TB disease in children, and one that allows the construction of likely effective regimens without a high occurrence of devastating side effects related to treatment, which can occur with injectable agents.

Pharmacokinetics of moxifloxacin and linezolid in children with MDR-TB and implications for paediatric dosing

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Moxifloxacin is one of the most frequently used fluoroquinolones for the treatment of multidrug-resistant tuberculosis (MDR-TB), and a key component of the newly recommended shortened (9–12 months) MDR-TB treatment regimen in adults and children. Linezolid is increasingly recognized as a potent antituberculosis drug. It was previously reserved mostly for extensively drug-resistant (XDR) TB, but in the 2016 updated guidance on MDR-TB treatment from the World Health Organization (WHO), linezolid has a more prominent role. Both moxifloxacin and linezolid are also components of multiple novel MDR-TB treatment regimens under evaluation. The pharmacokinetics of moxifloxacin and linezolid in children with TB have not been well described. The currently recommended dose of moxi-

floxacin in children is 7.5–10mg/kg once daily. The only published paediatric pharmacokinetics showed that in 23 children with MDR-TB aged 7–14 years receiving an exact 10mg/kg dose of moxifloxacin, total drug exposures (median AUC = 17.2 µg**h*/mL) were well below those seen in adults after the currently recommended dose of 400mg once daily (AUC = 40–60 µg**h*/mL); there is no published data in children < 7 years of age. The current WHO recommended paediatric dose of linezolid for MDR-TB is 10mg/kg/dose given thrice daily up to a maximum of 600mg; doses used in practice are lower (10mg/kg/dose twice daily if aged >10 years, once daily if aged >10 years) but have not been rigorously evaluated. Linezolid pharmacokinetics have been characterized in children with routine bacterial infections, but there is no data in children with TB and the dose in children that approximates exposures in adults receiving the dose most frequently used for TB (600mg once daily) is not known. We will present data from two ongoing observational pharmacokinetics studies in Cape Town, South Africa that are evaluating the pharmacokinetics and safety of multiple second-line antituberculosis drugs in HIV-infected and uninfected children with MDR-TB. Using population pharmacokinetic modeling methods we will characterize the pharmacokinetics of moxifloxacin and linezolid in children of all ages with MDR-TB. We will discuss the implications of this data for the optimal dosing of these agents in children in MDR-TB treatment regimens.

Predictors of MDR-TB treatment outcomes in children and adolescents receiving individualised regimens

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Background: Globally, over 30 000 children fall sick with multidrug-resistant tuberculosis (MDR-TB) every year. Without robust pediatric data, clinical management follows international guidelines that are based on studies in adults and expert opinion. We aimed to identify baseline predictors of death, treatment failure, and loss to follow-up among children with MDR-TB disease treated with regimens tailored to their drug susceptibility test (DST) result or to the DST result of a source case.

Methods: This retrospective cohort study included all children ≤15 years old with confirmed and probable MDR-TB disease who began tailored regimens in Lima, Peru between 2005 and 2009. Using logistic regression, we examined associations between baseline patient and

treatment characteristics and 1) death or treatment failure and 2) loss to follow-up.

Results: 211 of 232 (90.9%) children had known treatment outcomes, of which 163 (77.2%) achieved cure or probable cure, 29 (13.7%) were lost to follow-up, ten (4.7%) experienced treatment failure, and nine (4.3%) died. Independent baseline predictors of death or treatment failure were the presence of severe disease (adjusted odds ratio [aOR] 4.96, 95% CI 1.61-15.26) and z-score ≤ -1 (aOR 3.39, 95% CI 1.20-9.54). We did not identify any independent predictors of loss to follow-up.

Conclusions: High cure rates can be achieved in children with MDR-TB using tailored regimens containing second-line drugs. However, children faced significantly higher risk of death or treatment failure if they had severe disease or were underweight. These findings highlight the need for early interventions that can improve treatment outcomes for children with MDR-TB.

World Health Organization treatment guidelines for drug-resistant TB, 2016 update: recommendations and their application to children

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In 2015 and 2016 the World Health Organization convened experts to synthesize the current evidence base for the treatment of multidrug-resistant TB (MDR-TB) in children and to develop treatment recommendations which are directly applicable to them. The recommendations made relied heavily on observational studies although the availability of individual patient data did allow some adjustment to be made when exploring the effects of treatment. The recommendations are conditional and the certainty in the evidence remains low or very low. The presentation will discuss the process of developing these guidelines, and highlight the key recommendations on the use of both legacy drugs for shorter and longer MDR-TB regimens and the use of new drugs. The limitations of existing evidence in providing stronger and more specific guidance will also be discussed.

Background information: <http://www.who.int/tb/areas-of-work/drug-resistant-tb/treatment/resources/en/>

Challenges and solutions to scaling up paediatric MDR-TB treatment in Central Asia

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Management of pediatric drug-resistant tuberculosis (DR-TB) poses unique clinical, psychosocial and programmatic challenges. Major challenges include the non-specific nature of symptoms in children, difficulty in obtaining samples for microbiological confirmation, lack of uniformly followed guidelines to treat DR-TB in children, non-availability of pediatric friendly drug

formulations and paucity of data on safety of some drugs when used on a long term in children. Additionally, programmes are often under-equipped to respond to the significant psychosocial, socio-economic and developmental implications for children and their families resulting from such a protracted illness and treatment course. The experience gained in the National TB Programme/ Médecins Sans Frontières pediatric TB programme in Tajikistan, enabled us in finding some plausible solutions which could be applied in varied settings. Active case finding strategies like home visits with establishment of clear referral pathways, introduction of better sample collection techniques like sputum induction and standardized diagnostic facilities help in earlier diagnosis of the children. Prompt empiric initiation of DR-TB treatment while awaiting confirmation of diagnosis, liaising with pharmacists in drug-compounding and preparation of pediatric friendly drug formulations, appropriate monitoring for adverse effects of drugs, effective care of co-morbidities by integration of services and nutritional rehabilitation of children improve the quality of care. Programmatically, ensuring strong political will, establishing country specific guidelines, training, effective infection control measures, efficient supply, financing and record maintenance contribute vastly to the sustainability of improvements. Finally, the new WHO DR-TB recommendations provide significant new options, but also potential programmatic challenges.

23. Magnitude and scope of TB stigma: scale validation and cross-country comparisons

Overview of the TB stigma scale landscape: validity, utility and robustness of existing measures for use in measuring progress in reducing TB stigma

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A systematic literature review of the validity and reliability of TB stigma scales for various types of TB stigma (anticipated, enacted, internalized) is presented to highlight challenges and opportunities in measurement of the scope and magnitude of TB stigma. The methodological challenges are discussed and arenas for future research defined.

Stigma hotspots and time trends: mapping attitudes toward TB disease disclosure across 39 countries

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Repeat surveys of attitudes toward TB disease disclosure permit the monitoring of trends in TB stigma and GIS

mapping of TB stigma highlights hot spots for intervention. Socio-demographic correlates of anticipated TB stigma are identified across countries and regions.

Is attitude toward TB disease disclosure a valid proxy measure of anticipated TB stigma in the general population? Evidence from Honduras

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Willingness of individuals to disclose a family member's TB diagnosis is widely assumed to be a valid proxy for TB stigma and has been used uncritically in hundreds of demographic and health surveys. This study tested the validity of that assumption via a survey of Honduran presumptive TB clients using valid TB stigma and TB-HIV stigma scales.

Adding fuel to the fire: accounting for drug resistance and HIV in measurement of TB stigma

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The possibility of measuring TB stigma via scales and surveys across epidemiological contexts is problematized in this presentation which draws on qualitative studies in South Africa. The confluence of M/XDR-TB and HIV may complicate TB stigma measurement at the individual level.

24. Asthma and COPD: a shifting landscape

Challenges of using spirometry and peak flow measurement in low-income countries

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Control of airflow obstruction is hindered by lack of guidelines, unavailability and high costs of essential drugs and diagnostics like spirometer. Ungedared human resources to conduct lung functions on initial and follow up basis should not be neglected as an influential factor to management and control. Having lung functions diagnostics such as spirometer and peak flow meter at frontline of health system is essential yet low income settings face several challenges such as the non prioritisation of airflow obstructions and the suboptimal building blocks of the health system. High prices of spirometers and lacking of systematized training and quality assurance on spirometer and peak flow meter is a problem. Well-trained technologists at frontlines can improve success rates of testing among all age groups (< and > 40 years). Linking the reimbursement to high

quality testing to ensure accurate flow testing and interpretation hence optimal management and decision in conjunction to other clinical profiles and histories is challenging. Building on scenarios of BOLD studies and quality assurance and linkage with sophisticated research is needed to reflect on filed challenges and building pragmatic standard case management models.

A new paradigm for understanding and managing obstructive airways disease

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This talk will discuss the move from the out-dated and simplistic physiological concept of obstructive airways disease to a more meaningful and relevant paradigm that accurately reflects the observed heterogeneity and is more closely linked to selection of appropriate treatments.

Challenges of implementing new models of care in low- and middle-income countries

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Drawing on experience from Malawi, this presentation will cover the current provision of care for non-communicable lung diseases in Africa, explore possible solutions and challenges to their implementation.

Asthma and COPD: a continuum of disease from childhood: implications for low- and middle-income countries

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In low and middle income countries (LMICs), asthma and COPD are amongst the commonest non-communicable diseases occurring in children and adults respectively. Accumulating evidence suggests that exposures early in life, including exposure to cigarette smoke, indoor air pollution or early respiratory tract infections may predispose to the development of chronic respiratory disease including asthma or COPD. Birth cohort studies have shown that lung function trajectories are established early in life, further highlighting the importance of antenatal and early life exposures in determining long term lung health. This has major implications for health in LMICs where potentially harmful environmental exposures and the high burden of respiratory infections may cause acute illness, substantial mortality as well as a high burden of chronic respiratory illness.

25. Qualitative research for tuberculosis control: what lessons can researchers offer to policy makers and implementers in tackling drug-resistant TB?

Using qualitative research and stakeholder engagement to develop a patient-centred, psychosocial support intervention for MDR-TB care in Nepal

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Background: People with MDR-TB experience substantial anxiety and depression either as a consequence of drug side-effects or challenges of living with MDR-TB. Given the extent of mental health problems faced by patients, there are few studies exploring this issue. This study aimed to contribute for effective management of DR-TB cases through development and implementation of locally feasible supervision and patient support approach in existing DR-TB programme.

Method: The study used qualitative methods to identify the need and inform development of an intervention to improve psycho-social well-being of MDR-TB patients. In-depth interviews and focus group discussions were conducted with patients, family members, and providers. Drawing on the qualitative findings, evidence review and expert opinion, intervention components were identified to address the determinants of psychosocial wellbeing and intervention model developed aiming to reduce psychosocial burden of the patients and their family members. Interventions included psychosocial counselling using Healthy Activity Programme (HAP) that takes into account the patient's individual needs and tailored support, particularly in terms of the level of social support, depression and anxiety experienced by patients. The intervention also included improved health education using Information education and communication. The developed intervention model was tested in two centres and eight sub centres and assessed using qualitative approaches.

Key Findings: MDR-TB leads to major disruptions to patients' social and economic circumstances. Though mental health issues are common, the current MDR-TB programme rarely addresses these issues. Psychosocial interventions in routine TB programme are feasible and acceptability of the intervention is considerably high. However, length of time is critical for patient engagement. Within current resources and settings, it is challenging for the DOTS providers to deliver all the screening and psychosocial interventions in their regular work. The HAP module was successful to reduce the psychosocial burden among patients.

Conclusion: Where there is an urgent need for feasible and innovative psychosocial interventions to help MDR-

TB patients cope with their treatment, it is possible to screen and deliver HAP in routine National TB programme. However, HAP module needs to be further adapted to be delivered in the routine MDR-TB management programme.

'I have become a nothing': exploring the role of men's shame in undermining better health outcomes in men infected with TB and HIV, rural Zambia

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In 2014, a secondary analysis of ethnographic data, collected in 2006-7, was conducted. The primary ethnographic data followed 9 TB patients in 8 rural households in Southern Zambia during TB treatment. 7/9 were co-infected with HIV; 5 patients died. The secondary analysis used a western psychotherapeutic approach to identify worries of household members and explore gender roles and responsibilities, also drawing on quantitative household data and researcher reflections. Findings highlighted that men TB patients were particularly distressed due to their reduced capacity to provide food for their families. Experiencing a diminished sense of self and faced with a heightened sense of shame, men were more likely to suffer poor relationships, experience profound feelings of isolation and take up maladaptive behaviours which could cause significant harm to themselves, women and children. Systemic mental health research is needed to address shame experienced by men TB patients.

'At the district level there is still a large gap. . .': a qualitative research of implementation process of public private partnership for tuberculosis control in India

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As the Indian Revised National TB Programme (RNTCP) moved into the third phase of its implementation, partner organisations experienced crucial developments in the government's changing approach towards their involvement in confronting tuberculosis. Their identity as partners was well recognised at national level within the strategy of Public Private Partnership (PPP), however, the same understanding was not witnessed amongst the frontline implementers resulting in barriers to partner relationships. Drawing mainly on 'observations' & 'informal interactions' and supported by in-depth interviews, two examples (lab based & field based) from the ethnographic fieldwork will be presented and discussed. This paper argues that applying qualitative research

methodologies can enable a better understanding of the complex process of policy implementation. A closer understanding of these processes can help bridge the gap between field-level practices and central policy intentions, facilitating a move towards more effective partnerships at the district and sub-district level.

Lessons learnt from qualitative research in TB control in Nepal

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Drawing on the process of undertaking qualitative research into issues of TB control in Nepal - into the impact of Global Fund funding on programmatic performance, the roll-out of GeneXpert, and the experiences of tuberculosis amongst PLWHA - this presentation explores a series of inter related issues. First, the question of organisational and network partnerships in both undertaking and operationalising research; second, the experiences of institutionalising research amongst research partners both in practice and through running a series of experiential workshops; and third, the relationship between generating research findings and changing policy and practice.

Confronting resistance: positioning qualitative research in relation to global tuberculosis control and research

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The creation of successful global tuberculosis (TB) research and control strategies to combat multi-drug resistance (MDR) requires the scaling up and down of various objects (e.g. policy instruments, national programmes, drug regimens, equipment and staff, research etc.) in countries across the world. In order to reflect on these global efforts and how qualitative research can be used to examine them in diverging ways, this paper draws on my experiences as an epidemiologist and qualitative researcher on two MDR-TB studies in South-East Asia. It proposes that the positioning of qualitative research can lead to insights that resist the current paradigm of global TB control, such as how patients and health staffs' experience of MDR-TB care cannot simply be reduced to issues of control, and ultimately calling into question the limits and ethics of an emphasis of global control over care.

26. Best practices and challenges in ending TB in correctional facilities

Impact of TB transmission in prisons to the community

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Tuberculosis (TB) rates among prisoners are more than 20 times that of the general population in Brazil, the proportion of all tuberculosis cases occurring among prisoners in Brazil doubled from 4.1% to 8.2% from 2007 to 2013, due to rising tuberculosis incidence and incarceration rates. In a cohort study, we found an annual risk of tuberculosis (TB) infection of 26% (95%CI 23–29%) and incidence of active TB of 1771 (95%CI 1115–2614) cases per 100 000 population. Incarceration was associated with TB in an urban population; 54% of *Mycobacterium tuberculosis* strains were related to strains from persons in prisons. The high rate of incarceration and movement combined with extraordinary infection rates, indicate that prisons can be important reservoirs of TB transmission to the general population. Urgent new approaches are needed to control TB in this high-transmission setting.

Early case-finding and its impact on the TB burden in prisons of Azerbaijan

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Background: Early case finding is the cornerstone for tuberculosis (TB) transmission reduction and treatment success. The Main Medical Department (MMD) of the Ministry of Justice (MoJ) of Azerbaijan has provided health care to inmates for more than 20 years, and is a WHO Collaborating Center for prevention and control of TB in prisons. We assessed the impact of improved systematic screening to TB burden in penitentiary system (PS) of Azerbaijan.

Methods: During 2009–2011 case finding strategy in Azerbaijan PS included the mass screening and incomplete passive case finding. During the period 2009–2011, the cases with presumable TB identified based on symptoms did not have access to initial diagnostic test resulted with only patients on advanced stages of TB disease were transferred to Prison TB Hospital for diagnosis and further treatment. Mass screening was implemented annually via standard questionnaire and chest x-ray with further smear microscopy and or culture on solid media as an initial diagnostic test. In 2012,

weekly transportation of sputum samples from clinically identified presumable TB cases for Xpert® MTB/RIF testing was introduced in all prisons ensuring early TB case finding, complimentary to the annual mass screening. Since 2012, entry screening with standard questionnaire, chest x-ray and Xpert testing was introduced in the general prison hospital. All identified cases were treated with WHO-recommended treatment regimens.

Results: Number and proportion of identified smear positive TB cases, rifampicin resistant TB cases and cases with BMI < 18.5 kg/m² decreased significantly in PS of Azerbaijan after introduction of enhanced case finding strategy. Treatment success with first-line drugs among new bacteriologically confirmed TB cases increased significantly.

Conclusion: Early case finding through systematically applied enhanced screening algorithm significantly decreases the TB/RR-TB burden and improves treatment outcomes in PS.

Results of TB treatment and care for ex-prisoners in Republic of Moldova

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An important public health issue is the continuity of tuberculosis treatment after release because it often happens that detainees supervision is lost and they do not complete the treatment initiated in prison. Since 2007, the NGO 'AFI', implements in Moldova the support program for detainees with tuberculosis that require further treatment after release. The preparation of the prisoners starts while they are still in detention by completing the questionnaire of social needs. Afterward, with the help of the organization's social assistant is done the connection with the health system at the place of residence of the prisoner after release. During 2007–2015, the share of prisoners supervision lost became 2 times smaller and the rate of success rose to the indicator achieved among the general population.

Optimisation of TB services in the prison system of the Ukraine

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The Ukraine is among the top five countries with the highest M/XDR-TB rate. So the optimization and efficiency of the National TB Control Program is one of the most important medical and social problems of Ukraine and it is one of the priorities of the state health and social policy. This is due to the complex epidemiological situation, considerable expenses of the State budget for the detection, diagnosis, treatment and rehabilitation of TB patients. Like in other countries the burden of TB and HIV associated TB in prison is times higher than in the country overall. Persons who are in correctional facilities of the State Penitentiary Service

of Ukraine (GPTS) are at high TB risk group. The organization of effective and affordable TB care in GPTS of Ukraine is of great importance in the National TB control Program. Continuing social economic and political crisis led to decreased budget for healthcare in correctional facilities. In the context of reforming of the Health Care System and GPTS of Ukraine it is important to optimize the TB control system. Today in Ukraine TB control system reform concept which based on the best international experience and practices is developed with a focus on enhancing the role of outpatient care, laboratory network optimization, public motivation for timely access to medical care if TB symptoms. The protracted socio-economic and political crisis in Ukraine, resulting in inadequate funding for the National TB Control Program, the international technical assistance of GPTS of Ukraine partners has important role. So, Prison Healthcare System including TB services for inmates has been optimized to implement cost-effective interventions.

27. MDR-TB and XDR-TB treatment service delivery models in Africa and Latin America

Mixed ambulatory and in-patient treatment model of care: Ethiopian experience

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Background: Ethiopia is among the 22 high TB burden countries, and MDR-TB service accessibility is low. A mixed MDR-TB model of care where by patients initiate treatment in hospitals named as treatment initiating centers (TICs), and discharged to treatment follow up centers, the nearest health center for directly observed treatment (DOT).

Intervention: The Amhara and Oromia regional health bureaus with the support of the USAID-funded HEAL TB project decentralized MDR-TB services starting from January 2012. . TICs were renovated/expanded; a sputum sample referral system implemented; and clinical mentoring and continuing medical education provided.

Results: TICs increased from 1 to 22; annual testing for presumptive MDR-TB increased from 662 to 9597; and patients enrolled increased from 56 to 862. Three hundred eleven peripheral health facilities are providing DOT. Six-month culture negativity rate improved from 41.2% to 77.4%. The cure rate improved from 61.1% at baseline to 70.5% by Oct-Dec 2015.

Achieving rapid scale-up of MDR-TB treatment using a decentralised, mixed model of patient care in Uganda

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Setting: Uganda is among the 22 high TB burden countries with 47 000 TB cases annually. MDR-TB prevalence is estimated at 1.4% among new TB cases and 12.1% among previously treated patients. By 2012, there was an MDR-TB patient waiting list of over 300 due to health system constraints and lack of MDR-TB management capacity.

Intervention: The NTLP with support from the USAID-funded TRACK TB project built the capacity of the MDR-TB central unit and regional multi-disciplinary teams to provide ambulatory care and hospitalization. Patients were initiated on treatment at Regional hospitals and were transferred to lower level health facilities for daily DOT. Logistics support was provided for monthly clinical and laboratory evaluation of patients at the regional hospitals, TB infection control, health information systems, patient support, contact investigation, DOT supervision, coordination and quarterly cohort review.

Results: A 5-fold increase in the number of hospitals and lower level health facilities with capacity to provide MDR-TB DOT and a 12 fold increase in patient enrollment from 65 to 826 over 3 years; with optimal final treatment outcomes, TSR 74% and cure rate of 60% for the first annual cohort of 201 patients treated using this model.

Conclusion: The decentralized mixed model of MDR-TB management increases access, MDR-TB patient enrollment and achieves optimal outcomes comparable to hospitalisation. Further improvements are anticipated for subsequent cohorts through the quarterly cohort review and quality improvement activities.

Integrated home-based treatment of MDR-TB: South Africa experience

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There are approximately 12 000 MDR-TB patients initiated on treatment annually in South Africa. Treatment of MDR-TB patients was highly centralized. **Intervention:** A policy framework for decentralized and deinstitutionalized management of MDR-TB was adopted in 2011. This policy aimed at taking MDR-TB treatment closer to patients' homes to improve access to care and treatment success rates. The number of MDR-TB treatment initiation sites increased from 17

before 2011 to 645 in February 2016. There are 155 mobile injection teams that provide home-based care in areas where patients have difficulties reaching health services. There are 10 treatment sites where treatment is initiated by the Clinical Nurse Practitioners. The MDR-TB treatment success rate increased from 40% to 50% between 2010 and 2012.

Do decentralised treatment and care lead to better outcomes for MDR-TB patients? Results of systematic review

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Background: Management of MDR-TB is complex and prolonged, and has traditionally been provided in centralised specialised treatment centres. Community-based treatment promises to improve adherence and treatment outcomes.

Methods: We performed a systematic review and meta-analysis evaluates the evidence for the impact of community-based therapy, compared to centrally delivered treatment, upon patient outcomes and costs among patients with multi-drug resistant TB.

Results: Eight studies comprising of 4493 patients with MDR-TB were eligible for review inclusion. Two studies modelled cost-effectiveness, whilst the remaining six cohort studies reported on treatment outcomes and/or cost of health-care. Pooled relative risk estimates for decentralised versus centralised care for the outcomes of treatment success, loss to follow-up, death and treatment failure were: 1.13 (95%CI 1.01–1.27), 0.66 (95%CI 0.38–1.13), 1.01 (95%CI 0.67–1.52) and 1.07 (95%CI 0.48–2.40), respectively. Considerable study heterogeneity was seen amongst the studies for each pooled estimate.

Conclusions: Treatment success for MDR-TB patients improved when patients were treated in a decentralised setting, when compared to a centralised setting. Further studies, in a range of different settings, are required to improve the evidence base for recommending decentralised care for patients with MDR-TB.

28. Early warning system to improve patient access to TB medicines: from quantification to decision making

Project implementation strengthening country MDR-TB drug management and quantification in Belarus: strengths and weaknesses

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Belarus has the highest level of M/XDR-TB within the WHO Europe region. This project is aimed to strengthening country's ability to manage and forecast MDR-TB

drugs to ensure treatment for MDR-TB patients without interruptions. Belarus has a centralised governmental procurement system, warehouses, storage conditions, and system for drug supply and distribution. There are different forecasting and quantification methods used in country causing stock outs, expiry and irrational use of drugs. Comprehensive training for central staff was provided with particular attention to implementation of a new user friendly tool, QuanTB, to provide accurate forecasting and quantification and Early Warning System. In country training was organised for all regional key specialists resulting in a combined national forecasting. Currently a drug consumption module for the national electronic registry is under development which is envisioned to be connected with QuanTB.

Use of QuanTB: creating a constructive snowball effect en route to strengthen supply chain management of TB medicines in Bangladesh

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Present how QuanTB became the pivotal tool for quantification, forecasting and early warning system and most importantly discuss its larger effects on the supply chain management of TB medicines in Bangladesh since its introduction in 2014. Among the main benefits can be mentioned making regular procurement decision including planning, budgeting, ordering, and scheduling/rescheduling of supply from the Global Drug Facility (GDF), and adaptive changes for ensuring timely availability of medicines. Contributed to improve overall inventory management through standardizing of storage condition, creating expiry tracker for efficient distribution and contributing to avoid stock-outs or wastage. Providing accurate reports to relevant stakeholders on actual and impending medicine expiry and shortage. Tracking actual patient enrolment against assumptions (especially for DR-TB) when different regimens or medicines are used. Help tracking proper dispensing and compliance with guidelines in the facility level. Promoted increased coordination among stakeholders on procurement and supply issues.

Use early warning system for effective planning of resources and to improve access to TB medicines: experience of Rwanda and Somaliland

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Inadequate procurement planning and limited skilled staff to conduct quantification for TB drugs are challenges faced in Rwanda and Somaliland. Delays in the procurement process has led to stock-outs, and overstocking has led to expiries of TB drugs in the past. The presenter will show the applied approach of capacity building on TB drug management and quantification through regional training and in-country technical

support and the evidence-based decisions taken for effective planning of resources based on the use of an early warning system.

Managing risks of stock-outs, wastage, overstocks and expiries of TB medicines in Tanzania

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Tanzania is among countries benefiting from the Global Fund support in implementing TB control activities. In 2012, the country signed Transitional Funding Mechanism (TFM) grant to cover the period 2012–2014. In order to allow the TB program to continue implementing planned activities while waiting for New Funding Model to be approved, Global Fund approved Bridge Funding which included funds for procurement of TB related commodities. However, procurement of TB medicines was delayed by suppliers despite initiating the process early. This contributed to critical shortage of adult first-line TB medicines (FLDs). Apart from FLDs shortage, the country also experienced slow enrolment of MDR-TB patients than the number planned in 2015 and slow uptake of pediatric TB medicines which led to potential overstocks. The presentation will discuss how Tanzania used QuanTB for decision making and take appropriate actions to prevent stock-outs while also minimizing wastage.

Early warning systems for streamlining Global Drug Facility procurement services

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Medicines for treatment of MDR-TB remain expensive as lack of data for forecasting, quantification, and supply decision making results in hectic procurement, order cancellations, and treatment interruptions. The Global Drug Facility (GDF) and partners have been championing the establishment of data-driven early warning systems (EWS) in countries feeding into global forecasting and EWS. Improved country systems mean evidence-based forecasting and ordering, allowing the GDF to be more efficient in order consolidation, supplier engagement, and ultimately lead to stronger and stable markets and medicines price reduction.

29. Moving towards integrated community and primary health systems to improve outcomes for women and children affected by TB and TB-HIV

Child TB case finding and prevention at the community level in Uganda

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Uganda in recent years has strengthened childhood TB activities, by forming a technical working group including key stakeholders from TB, HIV and MNCH, developing guidelines and implementing training to decentralize diagnostic and management capacity for child TB to lower level health facilities. Two projects will be presented that target the existing community platform through engagement of Village Health Teams. DETECT Child TB implements routine household contact screening and preventive therapy. Under the lead of the Maternal and Child Health Programme Uganda is implementing integrated community case management (iCCM) of common childhood illnesses that was adapted by WHO and UNICEF to include risk assessment for both TB and HIV to increase case finding.

Joining the country dialogue on integration

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What does childhood TB integration mean from the perspective of different stakeholders including TB, HIV, nutrition, maternal and child health, government and implementing agencies? What are jointly defined opportunities, mutual benefits as well as evidence gaps and barriers to inform implementation and scale-up? What components of the health system are involved in and/or affected by the integration process and how? What is the extent of childhood TB integration and what is needed to move integration forward? This presentation will provide examples from country case studies on childhood TB integration in Malawi and Uganda.

Integrating TB services within the reproductive, maternal, neonatal and child health platform

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Reproductive, maternal, neonatal and child health services provide an opportunity to enhance access to TB prevention, diagnosis and treatment for HIV-infected and HIV-uninfected women and children through integrated service delivery. The World Health Organization is developing a toolkit to facilitate integration. It consolidates existing WHO recommendations for the prevention, detection and management of TB in women and children, best practices, operational experience and

job aids to facilitate integration. The toolkit is currently being piloted in the sub-Saharan African setting. This presentation provides an overview of the toolkit as well as experience and lessons learnt from piloting the tool to date.

Health systems thinking around TB integration

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Moving away from vertical to integrated TB programming, from pilot projects to sustainable scale up demands rethinking and restructuring of different aspects of a complex system. It involves policy makers and implementers from different programmes and disciplines. The presentation will consider needs for harmonization and coordination of policies, financing mechanisms, human resources, supervision, quality assurance, and health information systems.

Strengthening community and primary health systems for TB

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A lot of the discourse and push for decentralization of childhood TB prevention, diagnosis and care as well as better integration with maternal and child health and other key programmes is led by the TB community, while there are parallel efforts by other sectors and broader initiatives to strengthen district and primary care systems. A meeting of stakeholders from MNCH, nutrition, HIV and TB was held in New York in June 2016 to discuss our understanding of integration, opportunities and ways forward to move towards integrated service delivery. The presentation will share the outcomes of the meeting, and proposed actions for childhood TB integration as part of strengthening primary health systems.

30. Resistance to public health policy, the unique vector: tobacco industry

Status report on global and national measures to prevent tobacco industry interference in health and tobacco tax policies

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This status report provides an overview of progress by the WHO FCTC Parties and global partners to protect health policies from tobacco industry (TI) interference. Latest trends on TI interference show aggressive tactics are increasing while the progress rate by Parties to limit interference is piecemeal with many gaps still to close.

This industry interference takes place in a context whereby governments are struggling with a growing burden of preventable diseases, low tobacco taxes/prices, high tobacco use and rising health costs borne by health systems and future generations. The main threat to tobacco control is the TI's multi-pronged attack to deny, delay and minimise efforts to: reduce prevalence and affordability of tobacco; and to delay raising tobacco taxes with potential to direct revenue towards underfunded health programs. Multiple tactics are part of industry's global strategy to undermine government action using legal and economic threats with little reliable evidence and transparency. On the positive side, comprehensive resources based on FCTC Article 5.3 guidelines have been developed in recent years including toolkits for government, indexes by partners for comparing interference and progress in countries. Latest global reports on FCTC progress indicate Parties are doing more to support Article 5 and to both strengthen and counter interference in health strategies. Most progress, however, is incremental rather than comprehensive with a focus on: raising awareness of interference; monitoring the multiple opposition tactics; implementing national guidelines for public service officials; and developing research agendas to identify gaps in economic evidence for countering industry myths. A growing number of case studies demonstrate the important role of leadership in developing regulations, models and steps towards preventing or limiting industry interference. Lessons learned are that Parties urgently need to: implement regulatory measures consistent with FCTC Article 5 and 5.3 guidelines to protect their own health policies; and to monitor, expose and counter the claims that tobacco control will for example, harm government revenue, businesses, trade, the poor, tobacco growers and users. With the support of the FCTC, civil society collaboration and success stories, governments are slowly recognising the economic benefits of putting health goals ahead of industry opposition.

Countering tobacco industry interference in tax policies: successful strategies

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Increasing taxes on tobacco products is one of the most effective ways of decreasing smoking prevalence as stated in Article 6 of the WHO's Framework Convention on Tobacco Control (FCTC). This presentation will cover some of the main tactics used by the tobacco industry to stop or minimize tax increases as well as ways to deal with them. Being aware of such tactics and monitoring the industry will help deal with industry attempts to influence policy. Successful experiences in other countries can also both expose the inaccuracy of many of the TI's claims and help to counter them. Industry tactics have included: arguing that tax increases will not increase tax revenues, mainly due to increases illicit trade, will harm tobacco farmers, those who work in tobacco manufacturing and/or in the retail trade sectors.

Increased mechanization of cigarette production and consolidation of the industry have much more to do with economic dislocation than tobacco taxes. TI also argues that tobacco taxes hurt the poor disproportionately (poorer people spend more of their incomes on consumption, so pay a larger proportion of their income for all consumption taxes. Although these arguments are mostly unsupported by independent analyses, they are constantly reused in other countries. Tobacco companies also use pricing strategies to bolster their arguments that tax increases will adversely affect revenues and/or illicit trade. These can include: increasing or decreasing retail prices more or less than a tax increase (over or under shifting), the of timing price increases before or after a tax increase to manipulate sales and revenues and stockpiling to increase sales before a tax increase in order to show a drop in sales afterwards. An increasing number of countries are successfully countering these arguments using the experience from other countries, independent research, and monitoring of TI activities.

Observatory to monitor the strategies of the tobacco industry in Brazil

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The establishment of an Observatory in Brazil to monitor tobacco industry interference is an important step for protecting health policies from industry interference. In March 2016, CETAB/Ensp/Fiocruz launched an academic resource that explores how the tobacco industry influences policy and public health in Brazil. This tool will address several aspects about understanding of current and future approaches of the tobacco industry, the way it attempts to or interferes with public health policy development. The main task is inform governments and policy makers which are these tactics and to try to prevent such interference. The operation of the Observatories will be based on the method developed by the University of Bath in the UK (tobaccotactics.org), and will rely on a 'Wiki' approach that explores how the tobacco industry influences policy and public health in the relevant jurisdiction and internationally. The information collected, as well as the know-how on how to monitor the industry is being broadly distributed, among the Parties to the Convention, as part of the reporting system of the WHO /FCTC or otherwise. The Observatory Tobacco Industry Strategies in Brazil was created with support from National Commission for implementation WHO/FCTC (CONICQ), Pan-American Health Organization (PAHO), the International Union Against Tuberculosis and Lung Diseases (The Union), Framework Convention Alliance-Brazil (ACT), a well-known non-governmental organization already involved in counteracting the tobacco industry. Now, the Secretariat FCTC is giving a new financial support and has used the Brazilian Project as a model to others countries, mainly to the BRICS countries, considering that are home to more than 40% of the world population. Following this

initial step, the Brazilian team is populating the Platform with more documents that will give comprehensive and up to date information about tobacco industry. The Observatory is available in cetab.ensp.fiocruz.br

Public health policy and industrial epidemics: tackling conflict of interest, promoting policy coherence

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Public health policies have increasingly been conducted via partnerships with commercial sector actors, both in many national contexts and in global health. This approach is problematic in the context of non-communicable diseases, understood as industrial epidemics that are shaped by unhealthy commodity producers. Tobacco control has therefore developed a distinctive model of health governance centred on recognition of a fundamental conflict of interest with tobacco companies. This presentation considers the potential applicability of this model in other contexts, lessons from the WHO Framework Convention on Tobacco Control, and implications for policy coherence in addressing the Sustainable Development Goals.

31. Building research capacity in tuberculosis: the experience of training programmes and their impact in low-middle income countries

An NIH Fogarty clinical research training programme: achievements and lessons learned over 10 years

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Over the last decade, the NIH Fogarty Center has supported a collaboration between Emory University, Atlanta, Georgia and the National Center for TB and Lung Diseases in Tbilisi, Georgia focused on clinical research training in TB. We report here on our experience in providing research training to trainees from the country of Georgia utilizing a model of combining didactic long distance training (via videoconference), in country graduate education, and intensive mentoring over a two-year period. We highlight the successes of the program including the productivity of >20 long-term trainees during and after their training in regards to publications (>50), grants, and career advancement. Just as importantly, we also discuss past and current challenges in regards to attracting and retaining trainees, skills development, attaining funding, and developing in country mentorship. Our experience demonstrates the significant potential of a collaborative clinical research training program while highlighting challenges to sustainability.

SORT IT model: successes and challenges

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SORT IT (Structured Operational Research Training Initiative) model, developed by The Union and MSF in partnership with WHO-TDR, and is designed for building operational research capacity in low and middle income countries. It is an output oriented course which combines teaching with implementation. Course participants are guided through the development of research protocol, data management and scientific writing and mentored through till the research gets published. Till date, about 400 participants from ~75 countries have attended SORT IT courses and of them, more than 90% have successfully completed the course and published their research. Nearly half of these studies have been reported (self-reported by participants) to have impacted policy/practice. At 18 months post-course, about half of the participants report continuing to conduct/publish OR and about one-third report having facilitated in other OR courses. Challenges relate to delayed ethics approvals, intense mentorship requirements and need to incorporate qualitative research methods.

From different angles: role of research training programme for personal development and scientific research capacity building at the National Center for Tuberculosis and Lung Diseases (NCTLD)

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After dissolution of Soviet Union, the Georgian Health-care System faced limited funds, inadequate legal and ethics framework and institutional capacity for clinical research. Being a high TB burden country, Georgia received a unique opportunity to train TB clinical research scientists through Emory Georgia TB Research training Program (EGTB RTP) since 2005. The program has supported scholarships for > 20 research trainees who eventually took the leadership in TB control of the country, and recently led to the creation of a clinical research unit at NCTLD in 2014. With stepwise personal carrier development I have led to this process for several years, supported with mentorship by Emory University senior faculty. I direct our research unit which currently runs 33 research projects in collaboration with leading European and US Institutions. Strengthening of research ethics and legal frameworks along with sustainable local funding are needed for further enhancement of research capacity in Georgia.

32. Should addressing tobacco use in TB and HIV patients be integral to disease control programmes? A case for support

Prevalence of tobacco use in TB and HIV patients: secondary analyses based on demographic and health surveys and literature review

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We present the findings of two studies estimating the prevalence of tobacco use among individuals with HIV and TB in high-burden low and middle-income countries (LMICs) countries Study-1 is a secondary analysis of the Demographic and Health Survey data from 28 LMICs. For each country, the prevalence of tobacco use among HIV-positive individuals was compared to general population. Study 2 is a systematic review that searched several literature databases for eligible studies. Data were extracted and smoking prevalence among individuals with TB was estimated. In Study 1, the prevalence of tobacco use among HIV-positive individuals was consistently higher than the general population prevalence for both men and women in all 28 countries. Study 2 identified 180 records. The prevalence of tobacco smoking in individuals with TB ranged from 15.2% to 70%. There is need for specific tobacco control interventions targeted at individuals with HIV and TB in high-burden countries.

Digital health interventions for TB tobacco control

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TB and tobacco consumption are leading global causes of disease and death. Smoking predisposes to TB infection, reactivation and recurrence of TB, and dying from TB. Health risks linked to both conditions are to a large extent modifiable through preventive and curative interventions which can be implemented at population level, in alignment with the vision of WHO's End TB Strategy. Digital technologies provide opportunities to increase the scale of such efforts in different ways, made increasingly possible by the wider availability worldwide of computers and smartphones, and networks of Internet and mobile telephony. The speaker will use examples of how digital health approaches are being used against TB and tobacco through support to patient care, programme monitoring and management, and human resource development. The presentation will also discuss the evidence underpinning such interventions, the knowledge gaps, and avenues for future. It will also highlight how professional groups such as The Union and the European Respiratory Society can play a pivotal role in supporting further the innovative, digital technologies and the gathering of evidence about their effectiveness.

Background information: <http://www.who.int/tb/areas-of-work/digital-health/en/>
<http://erj.ersjournals.com/content/early/2016/05/26/13993003.00424-2016>

Innovations for TB-tobacco: mHealth

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TB and tobacco smoking are currently two formidable concerns, and independently pose considerable threat to global health. There is adequate evidence to conclude that an integrated approach towards TB-tobacco prevention and treatment can be beneficial for prevention of both the diseases and confer advantages on the lung health of TB patients who quit smoking. The rapid and unprecedented growth of mobile phone ownership and usage across low and middle income countries (LMICs) presents opportunities for cost-effective, convenient and broad-reaching strategies for TB-Tobacco control. The presentation will discuss World Health Organization (WHO) and International Telecommunication Union's (ITU) joint initiative on mHealth for TB-Tobacco, developed to promote behaviour change in those TB patients who use tobacco to quit tobacco use and provide support through the course of their TB treatment, using text based messages. The program intends to cover the spectrum of cessation advice and tries to increase awareness of on-going TB treatment and enhance treatment adherence.

TB and tobacco control integration in primary care: WHO/The Union recommendations and country experiences

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Smoking has causal associations with TB incidence and outcome, accounting for more than 20% of global TB incidence. Therefore, the National TB Programme (NTP) and the National Tobacco Control Programme should strengthen their collaboration to achieve mutual benefits. WHO and The Union developed policy recommendations and identified intervention models on how to integrate TB and tobacco control measures in primary care in 2008 through the publication of the WHO/The Union Monograph on TB and tobacco. Although NTPs could reach > 1 million TB patients who use tobacco per year, TB care providers' provision of cessation services is low due to lack of supportive systems in majority of countries. The experiences of WHO country projects show that integration in primary care is feasible and effective. From 2013 to 2015, four countries (Cambodia, India, Nepal and The Philippines) joined WHO project. 799 TB patients who use tobacco received brief tobacco interventions and 31.9% of them quit successfully for 3 months. 5115 patients with respiratory diseases also received brief tobacco interventions. The author will first introduce the recommendations, the potential impact of

brief tobacco interventions in TB programme and WHO technical resources. The author will then present country experiences and next steps in advancing this joint work at country level.

Scaling-up TB-tobacco integration at global level-mobilisation of resources

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Tobacco Control integration within TB programs will ensure better case management as a whole like delay in seeking care, default, smear conversion, disease severity, acquired drug resistance and mortality during and after TB treatment. This will lead to better economics for TB programs. Smoking cessation will further protect the patient and the family members from other related diseases like cancer, COPD, CVD and strokes. However, resources need to be mobilized to ensure integration at national and global level to address this dual epidemic of TB and NCDs.

33. The growing gender gap in TB: a consequence of resistance to recognising men's vulnerability in TB diagnosis and care?

A patient's perspective

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Men's barriers in accessing TB diagnostic and treatment services are rarely discussed, and the fact that a TB diagnosis impacts men in gender-specific ways is seldom acknowledged. A former TB patient who has experienced these difficulties first hand will speak about his experience, highlighting the challenges he faced in seeking and accessing diagnosis and treatment and the personal, financial, social and familial impact that TB has had on his life.

Gender differences in TB burden and care pathways

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TB notifications are usually higher in men than women, and prevalence of disease is significantly higher among men. Both genders are affected by a complex network of biological and socio-cultural risk factors, and differences in healthcare utilisation are also apparent, with comparisons of prevalence and notification data suggesting that in many settings men are disadvantaged in seeking and/or accessing TB care. Among those who do access diagnostic services, there is evidence that men are less likely to initiate and complete treatment, resulting in worse outcomes. Men and women both face specific and

substantial barriers to care, but loss to follow-up is greater among men, who remain infectious in the community for a longer period of time. Case studies utilising mathematical modelling to explore gender differences in the TB care pathway in Malawi and Viet Nam will be presented, emphasising potential opportunities for intervention to improve gender equity.

The influence of masculinity on care-seeking for TB

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More men than women die from, or are notified or remain un-diagnosed in the community with tuberculosis (TB). The model used to detect, manage and prevent TB globally relies on self-presentation by patients at health facilities, or passive case-finding. Why men remain un-diagnosed with TB disease is poorly understood. We carried out a study to understand why men do not seek healthcare when having TB-related symptoms, focusing on chronic cough, a known TB symptom. We framed the study within Connell's conception of masculinities, and also the broader social constructionist perspective, paying attention to how these approaches adopt historically and culturally specific forms of analysis, and acknowledge the construction of the world through daily interactions, as well as the possibility of multiple and contradictory creations of the world. Data were collected using focus group discussions and individual interviews with men and women who were selected from among the general community, TB patients, coughers who had not sought formal care, and healthcare workers, within an urban setting in a low-income country where informal employment was near-universal, and HIV-prevalence, HIV-TB coinfection and ART coverage are high. Images and roles expected of or desired by men included being a material and economic provider, and having control and self-determination in life. These images were, however, threatened by unstable and low employment levels and incomes, and illness. In their pursuit of the socially valued yet elusive representations, men often found themselves engaging in complex, often-compelled but sometimes internalized and thus somewhat unconscious, choices that involved relegating their own health. Additionally, health system-related challenges, specifically shortages of human, equipment, and drug resources, unprofessional conduct, and waiting times and procedures that inconvenienced or emasculated men, were described as deterring healthcare-seeking. Men are frequently held to have power and advantage relative to women. This study reiterates how a combination of various structural factors that include gender role expectations, limited incomes, health systems problems, and high HIV-prevalence imply a special type of vulnerability for men. Male-sensitive approaches to improve utilization of TB services are therefore needed.

Strategies for reaching men through occupational screening in Lagos

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Background: Globally, including Nigeria, efforts and strategies for TB control are continually targeted towards the perceived 'vulnerable' groups, women and children. Annual TB notifications have repetitively shown a greater proportion among women than men mostly within the economically productive age of 15–59 years (WHO 2011–2014 report). Contrarily, the 2012 National TB prevalence survey revealed more TB in men... 'an irony of focus'. Limited access, care seeking behavior and strategies for TB control are but a few of many probable causes for this growing gender gap in TB (NTP KAP survey 2012).

Objectives: To describe the process currently being undertaken to improve access to TB diagnosis among men.

Methods: Comparative analysis of the yield in age-disaggregated TB notification between 2015 and 2016, using a multi-faceted approach inclusive of record review of TB case notification, Mapping of male-dominated industries and congregate settings, Engagement-Intent-driven-Advocacy (EIDA) framework, situation analysis on available health services and its utilization in the industrial facilities, purposive sampling of industrial sites for engagement and strengthening of TB surveillance services, and routine TB screening adherence monitoring. **Strategies:** These involved engagement of large industrial companies, engagement of communication expert in developing and airing of men-targeted radio messages and conducting an in-depth analysis of different radio listeners, distribution of IEC materials at local football viewing centers, gambling sites and road transport workers forum (vehicular & motor bike garages), distribution of TB branded motor bike riders fluorescence-safety vest, engagement of labour union workers, capacity building and establish supervision, M&E systems linked to the NTP.

Results: Will be measured over a period of a year (2015 baseline against 2016). Indicators measured are; total number of men screened for TB, proportion of identified presumptive TB cases, M:F ratio of diagnosed TB and half-yearly incremental rate in TB screening adherence.

Challenges: Engagement resistance from large companies, difficulty assessing direct yield of targeted TB education messages to men, assumptions on ascertaining

the most listened radio station by men and confidentiality of staff/patient data in companies.

Conclusion: For a world-free TB, strategies need to be revisited to cater for the covert group, men.

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Advocacy for gender equity

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Despite epidemiological evidence that men have a higher burden of disease and are disadvantaged in accessing TB care, major donors and policymakers are resistant to the idea that interventions to promote gender equity must focus on men, and so TB policies and strategies on gender continue to target women. Broader efforts in advocacy will be necessary to bring about the paradigm shift that men ought to be included in gender analyses, discussions and strategies. The representation of 'gender equity' and how it is translated into practice will be discussed.

34. Monitoring TB treatment: alternatives to microscopy and culture?

Innovative non-culture methods for monitoring treatment response in tuberculosis

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We report results from the PANBIOME study that compared the value of MGIT with our innovative molecular bacterial load assay. This clinical trial, performed in four African centres in three countries demonstrated the applicability of the technology. It showed that the method could be used successfully to monitor treatment response. The major advantage of this approach was that results were generated in approximately four hours giving the potential to assist in patient management. The specificity of the assay meant that no samples were lost to contamination unlike culture based methods.

Monitoring host immune response a realistic approach to treatment monitoring?

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Although the specificity of host immune-markers is sub optimal for diagnostic use the host immune-marker kinetics may have application for following treatment. These markers are particularly interesting as they may be amenable to simple near patient measurement. The possible advantages and limitations of this approach will be discussed.

Monitoring drug levels during TB therapy a realistic goal?

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Therapeutic drug monitoring (TDM) is a tool to tailor the dose to the individual need of the patient to optimize drug exposure to increase efficacy and reduce toxicity. Although TDM has been advised for more than a decade, implementation has been difficult. TDM has been typically used in reference clinics, most frequent in well-funded settings. However, new innovations made TDM in combination with new evidence to support TDM will make it feasible in low income settings. A frame work is provided how TDM could be implemented. In addition, different analytical procedures and strategies to make a business case to finance TDM are discussed.

Is treatment monitoring as a test of cure realistic?

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A useful biomarker for cure would be one that predicts, in an early stage of treatment, relapse on a shortened treatment regimen. Culture conversion after 2 months of treatment is correlated with relapse-free cure but the method is cumbersome and slow and individual patient predictions cannot yet be made. Simpler biomarkers are needed but whether early individual prediction is at all possible depends on the valid mechanism by which relapses occur.

35. E-cigarettes and other electronic nicotine delivery devices: where are we now? Regulation, opportunities and protecting public health

Regulation on electronic nicotine delivery systems in different countries

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Similar to conventional cigarettes, the E-Cigs and other ENDS devices are subject to a range of laws and policies that differ from country to country. While some nations like Brazil, Norway and Singapore have banned ECs/ ENDS completely, there are many countries that still lack clear regulations. This talk will provide an overview of select country-level laws that regulate the sale, use, advertising, promotion, taxation and/or classification of e-cigarettes.

Opportunities offered by E-cigarettes

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Since electronic cigarettes were introduced in the market, there has been an ongoing debate on their safety and efficacy and whether they should be treated in same way as tobacco, as a stop smoking medication, or as a new class of products. While some studies claim e-cigarettes are not effective as smoking cessation aids, others support the use of e-cigs as a low-cost, effective intervention that could help millions of smokers stop using tobacco permanently. This session will explore the various opportunities offered by e-cigarettes and tobacco harm reduction in the context of comprehensive tobacco control.

E-cigarettes and FCTC articles

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The World Health Organization Framework Convention on Tobacco Control (WHO FCTC) is an international public health treaty providing a framework of tobacco control measures to protect present and future generations from the devastating health, social, environmental consequences of tobacco consumption and exposure to tobacco smoke. Both demand and supply issues are addressed through specific FCTC Articles. ENDS have the potential to undermine a number of these Articles. Article 5.2 addresses preventing and reducing nicotine addiction independently from its source. Article 5.3: Protection from vested commercial interests. The recent licensing by the UK Medicines and Health Care Regulatory Authority of a British American Tobacco e-cigarette is a current concern and controversy. The widespread marketing and promotion of ENDS, use of ENDS, and still-evolving science of the product's safety and use may also hinder implementation of Article 8: Protection from second hand smoke. Article 12: Denormalization of tobacco use. Article 13.2: Tobacco advertising, promotion and sponsorship bans. Article 14: Evidence-based treatment for tobacco dependence and cessation.

36. Demonstrated need for strengthened national Stop TB partnerships

Identifying TB champions

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Nigeria has the highest TB burden in Africa, and is one of the world's 22 high-burden TB countries. With a very low case detection rate (less than 15%); high TB-HIV coinfection; over 170 000 annual TB-related deaths; and very low domestic funding for TB; Nigeria definitely needs the political support at all levels to end TB in the country. Confronted with these challenges, Stop TB Partnership Nigeria is working with all stakeholders to end TB in Nigeria by advocating for increased political commitment of all tiers and levels of government; increased public awareness and funding for TB programs at the national, state and local governments levels. Stop TB Partnership Nigeria is the multi-stakeholder partnership complementing the efforts of the government and partners to end TB in Nigeria. The Partnership was established in 2007 and though had so many challenges at the beginning that limited its viability and sustainability for many years; but with the commitment of all stakeholders within and outside the country, the Partnership is now more functional and has been improving in its efforts of contributing to end TB in Nigeria. Within a year of the new leadership of Stop TB Partnership Nigeria, it has recorded many achievements especially in improving the political profile of TB in the country. Specifically, Stop TB Partnership Nigeria was able to nominate and receive the acceptance of the Wife of the President (The First Lady) to be the TB Champion. This is extremely significant as it will not only improve political profile of TB at the country level but also high-level advocacy and engagement of the leadership at the regional and global levels. Also, Stop TB Partnership Nigeria was able to organize a very successful first National TB Conference that included other side events which attracted the support and participation of all stakeholders including high profile personalities at the national, regional and global levels. The TB Community Forum for civil society and patient representatives and the Nigeria TB Caucus for parliamentarians are also part of the success stories of Stop TB Partnership Nigeria.

Mobilising members of Parliament

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Stop TB partnership Kenya on the other hand has managed to mobilise Members of Parliament from Kenya to make commitments to the fight against TB. Courtesy of the efforts of the Partnership, 11 MPs have signed to a communiqué binding the MPs to the TB related declarations laid out in the document. With support from USAID, the partnership has also mobilised media to increase TB awareness. The partnership continues to mobilise the private sector to work within their core-competences to invest in the fight against TB. With more efforts and capacity building, national stop TB partnership will be the vehicles that will deliver countries towards achievement of the End TB strategy targets.

Partnering to implement the national TB programme

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The Philippine Coalition Against Tuberculosis (PhilCAT), founded amidst the realization that collaboration and partnership between the public and private sectors was vitally needed to succeed in the country's fight against tuberculosis, has been the partner of the Philippines Department of Health in the implementation of the National TB program (NTP) since 1994, specifically in engaging private providers. The Annual PhilCAT Convention held every August served as the venue for updating private and public health providers on the global and local TB situation and the recent developments in the diagnosis, treatment, prevention of tuberculosis. PhilCAT through the various consensus statements and clinical practice guidelines it has developed in partnership with the NTP and other professional associations had been instrumental in galvanizing private medical practitioners towards a unified standard management of TB. As a champion of the public-private mix (PPM) approach to TB control, PhilCAT led the way in scaling up the strategy nationwide. Following the successful pilot testing of DOTS in the private sector, one national PPM coordinating structure and sixteen (16) regional structures were set-up, around 6000 physicians were mobilized and trained in DOTS from 2004 to 2015 encouraging them to support and comply with the policies, guidelines and standards of the National TB Program (NTP). Furthermore, the partnership also participated in the 2013 and 2016 NTP Joint Program Review and the development of the Philippine Plan of Action to Control Tuberculosis (2010–2016) as well. From 2004 to 2008, efforts to attract support from the private sector have resulted to at least 36,870 all types of TB cases initiated to treatment, out of which, 15 892 were new smear (+) TB cases. The expansion of Hospital TB DOTS initiative has also been an important achievement of the partnership. In 2015, the 607 (318 private) hospitals engaged by PhilCAT as sub-recipient of

Global fund New Funding Model detected a total of 16 802 TB cases, 5.6% of the total cases detected by the NTP.

Engaging civil society in the fight against TB

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The Partnership for TB care and Control (PTCC) in India is a registered organisation that includes more than 200 CSOs working in the field of TB and TB- HIV for past many years. PTCC has brought together all these organisations working in isolation onto a common platform at the national scale. This has facilitated CSOs working in various remote areas to come forward and share their good practices and also raise issues that is impeding their work. PTCC has also been instrumental in providing a voice to the affected community for addressing concerns. Within the PTCC, we are in the process of establishing a network of TB affected community of which includes cured TB patients and patients undergoing treatment.

Strengthening collaboration between all partners and engaging with the country coordinating mechanism (CCM)

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Uganda Stop TB Partnership (USTP) is a NGO formed in 2004 to support and coordinate partners engaged in TB control in Uganda to contribute to one National TB program strategic plan. Monthly working groups meetings for DOTS expansion, TB-HIV, and ACSM meet and discuss and share experiences. On a quarterly basis USTP holds general meetings for all the partners and guidelines, policy documents and success stories are shared.

Overall Achievements by USTP:

Membership continues to grow every year and now has over 60 members.

For the last three years, has a fully functional secretariat which is supported by the Global Fund.

After the Union conference in Barcelona, addressed the parliamentary social services committee and the Barcelona declaration was signed.

Engaged the media fraternity in the TB response, and a media team formed.

For the last ten years spearheaded commemorating the World TB day at both national and district level in selected districts.

Supporting communications interventions on radio and TV.

Spearheaded the development of the National Communication strategy for TB.

Spearheading Public Private Mix (PPM) including development of national guidelines.

Taking part in Country coordinating mechanism (CCM) for Global Fund activities:

Participates in Community dialogue and constituency engagement activities and over sight visits. The site visits

have enabled CCM to analyze how the intended beneficiaries have been supported by the Global Fund and also helped to guide planning for services.

Lessons learnt:

A national partnership can be able to effectively engage partners to support the National TB strategic plan and contribute in a coordinated manner to the response.

Sharing experiences can help in informing the planning and programming for TB control.

Community dialogues are very useful in priority setting for the beneficiaries of the services.

Engagement of communities, civil society organizations, and public and private sector providers is quite possible.

The NTP's need the support of different partners.

Sustaining and strengthening National TB partnerships requires a lot of support from the registered members and government. Membership should go beyond the traditional TB or health related civil society and widen scope

37. Tackling TB in cities: lessons and best practices in urban TB

New strategies for reaching the urban poor with TB services in Dhaka, Bangladesh

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Background and challenges: Dhaka the capital city of Bangladesh has grown extremely rapidly over the past decade, and health services have struggled to keep up. There are multiple actors in the urban with different choices. Certain risk groups of people such as slum-dwellers, garment workers, prison inmates who are exposed to poor environmental conditions like overcrowding, poor housing, poor health and nutrition status one of the current priorities in national TB program is to develop a suitable TB program system in urban areas with complex structures of population and service providers of both public and private.

Strategies: Sputum campaign is being done in the large slums following mobilization through miking at previous day. Community health workers organize specific sputum collection centre in the slums for sputum collection and smearing. TB presumptive identified at different hospitals (in-door and out- door) are referred to laboratory of the DOTS corner established in hospital premises for sputum smear examination. Sensitization meeting with management authority and orientation programme with factory staff and workers is being done at factory premises.

Results: In 2015, 25% of total cases identified in Dhaka urban came from DOTs corners of different tertiary hospitals of Dhaka city, 24% from the graduate private practitioners, 7% cases from the factory workers and only 2.4% cases identified among slum dwellers which is still very low as we didn't have programme coverage all slums yet.

Conclusions and recommendations: Adopting efficient and effective approaches for the underserved urban poor

will enhance TB case findings. Political commitment and ownership is needed to sustain the existing best practices. Coordination with diversified partners in health and integration with them will improve effective tuberculosis control within changing urban environments. The partnership also helps the programme to identify the programme gaps and realize the need to improve its performance by strengthening the general health services.

Improving urban TB control throughout the Americas

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In 2014, the Population Division of the Department of Economic and Social Affairs of the UN estimated that by 2015 North America would be the most urbanized region in the world, followed by Latin America (LA), with rates of 82 and 80%, respectively. In LA the economic activity is concentrated in the cities (60-80% of GDP), the relative incidence of urban poverty is decreasing but the absolute number of poor people is increasing; one out of every four urban dwellers is poor and 27% of the population lives in slums with big inequity and inequality. The TB incidence in the Americas is declining, but there is a gap between estimates and notified patients. In 2014 there were more than 60 000 missed TB cases. The Regional TB Program (RTP) of PAHO/WHO analyzed where the TB missing cases in LA are and concluded that large cities concentrate most of TB patients. The RTP developed the 'Framework for Tuberculosis Control in Large Cities of LA and the Caribbean' composed by 8 components. Thanks to a regional USAID grant the RTP began the implementation of the framework in 3 pilot cities (Guarulhos, San Paulo-Brazil; Lima, Peru and Bogota-Colombia) that was later expanded to other cities of Colombia and cities in 5 other countries. During the implementation process we learned: 1) local and national authorities were unaware of the TB burden in cities; 2) the municipalities identified with higher TB incidence through epidemiological mapping had also the highest poverty rates; 3) segments of the populations living in the poor municipalities were among the TB vulnerable groups (indigenous, African descent, migrants, homeless, alcoholics, people with HIV and others); 4) the mapping of health care providers revealed that they were far from the poor populations. The analysis of health care showed that it was fragmented and not adequate for the needs of the population, 5) local and national social protection programs didn't include TB patients and the intersectoral approach in TB control strategies wasn't in the political agenda. According to the TB situation analysis the TB programs mobilized financial resources; coordinated the health providers; identified the population's requirements and adapted the care to their needs.

The Zero TB Cities Project, and lessons from expansion of the urban private sector model in Pakistan

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The Zero TB Cities Project aims to bring the global tuberculosis (TB) epidemic into the elimination phase, by focusing on local government participation to drive and maintain catalytic successes against TB in multiple locations. As an example of this approach, results from the recent, large expansion of the Karachi urban private sector model will be outlined, and lessons for the emerging Zero TB Cities projects in other countries and cities will be presented.

Networking urban private providers in Patna and Kolkata

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World Health Partners will present on two of its efforts in urban TB. First, in Patna, Bihar where WHP has contributed as a Private Providers Interface Agency (PPIA). The PPIA model addresses one of the major challenges in urban TB, which is to reach private providers and engage them fruitfully in the RNTCP program. WHP has created a service delivery ecosystem by engaging with a broad network of existing formally and informally qualified providers, pharmacies and laboratories using social franchising strategies, a low-barrier technology-based reporting platform and an inclusive system of incentives to motivate appropriate delivery of TB diagnosis and treatment. The project's success crucially hinges on integrated components consisting of sensitization of providers about importance of early diagnosis and case notification, and strengthening it with training on the standards of diagnosis and treatment. The program ensures the clients (TB patients) receive standardized services on a subsidized or no-cost basis. Its implementation has coincided with a 4-fold increase in the case notification rate. Second, WHP is implementing the THALI project in Kolkata, which includes a cross-sectoral effort on political advocacy, municipal capacity building, private sector engagement, and IT innovations to address the urban TB burden in this megacity. Innovative frugal alignment of existing resources, appropriate technology, institutional strengthening, incentives for complete cure, cost efficiency through volumes and high quality services, supported by 360 degree communications and advocacy, will underpin the project's improvised private sector delivery model. The project will address selected Kolkata slums directly and the whole city indirectly in collaboration with the municipal and state TB offices, prioritizing those areas with the poorest TB situation. In Kolkata, through formal and informal associations, will engage multiple levels of public-private providers in a tiered service delivery network in Kolkata, including Indian Medical Association (IMA), informal providers, chemists and private pathology labs. All participating providers will be

brought under the umbrella of the project, facilitating financial settlements between providers through an interlinked system (public and private). Additionally, program seeks to bring about the desired behavior change among providers to ensure appropriate TB case management. A multi-layered patient tracking mechanism ensures completion of treatment.

A multi-pronged strategy for tackling TB in Mumbai

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Mumbai represents 1% of India's population and registers 3% of total TB cases and ~13% of total MDR-TB cases of the country. Annually 30 000 TB cases are registered for treatment in Mumbai under RNTCP and 15 000 cases are notified by the private sector. In the last two years, Mumbai reported ~3500 MDR-TB cases each year. Key challenges include poor sanitation, infection control, overcrowding, poor risk perception, irrational treatment and unregulated private sector. The response to TB in Mumbai has been revitalized over the past 3 years, leading to a doubling of TB notifications. In March 2013, the city administration (MCGM) launched an ambitious 'Mumbai Mission for TB Control', which articulates 7 key strategies to achieve universal access to TB care: 1) Active case finding in slums, 2) Access to rapid diagnostics including universal DST, 3) Improving access to effective treatment, 4) Extending services and support to providers and patients in private sector, 5) Airborne Infection control, 6) Building empowered communities, and 7) Organizational strengthening. One of the most successful interventions has been a Private Providers Interface Agency (PPIA) which actively engages private providers including informal and formal medical practitioners, laboratories and chemists through a unique model. The Mission mode strategy has resulted in an improvement of overall TB services and an enhanced administrative capacity. However, with changing epidemiology, the progress of Mission was reviewed in terms of challenges and gaps based on which, an Action Plan is created for the next 3 years which focuses on commencing universal DST and DST guided treatment in phased manner, establishment of District DRTB Centres at peripheral centres, continue involvement of private hospitals/NGOs, sustain PPIA model through program strategies, intensified TB case finding and generating local resources by mapping partners and donors via integration with CSR. Mumbai has already initiated DST based treatment in 7 districts and is in the process of devising a concrete AIC plan. While Mumbai's TB response plan provides a roadmap for further transforming urban TB control, the immediate challenge is financing the intensified efforts and scaling up diagnostic capacities for DST.

38. The effectiveness and obstacles for social support for TB patients

Social support guidelines

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What is the rationale and evidence behind social support guidelines?

Effectiveness of social support on TB treatment adherence and treatment outcomes

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What is the evidence and what are the implications for implementation and research?

Effectiveness of interventions to reduce TB stigma

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Setting: Despite the progress made in tuberculosis (TB) treatment, the success of public health efforts is hampered by pervasive stigma. Manifestations can be social isolation, low self-esteem and discrimination. There is a strong need for effective evidence-based interventions, but no comprehensive review has previously been conducted.

Objective: This systematic review assessed the effectiveness of interventions aimed at reducing internalized, anticipated or enacted TB stigma in people with TB, healthcare workers, care givers and the general community.

Design: The main eligibility criteria for included studies were the evaluation of an intervention aimed at reducing TB stigma between 1950 and 2015. Databases searched were Pubmed, Cochrane Library, Ovid, Embase, PsycInfo, Sociological Abstracts, CNHA and LILACS WHO. Gray literature was obtained from the WHO database, STOP TB partnership website, STOP TB USA weekly digest, Centers for Disease Control and Prevention TB resource database, KNCV archives and the UNION conference on TB and Lung Disease from 2008-2015. We also used the snowball method not to miss relevant studies. Quality of evidence was assessed using the Downs and Black scale for quantitative studies and the Spencer framework for qualitative studies.

Results: Of the 4677 records identified and screened, only seven were eligible for inclusion. The four studies that primarily targeted anticipated stigma evaluated information campaigns aimed to the general communi-

ty, education of healthcare workers, support groups and TB clubs. The three studies targeting internalized stigma assessed the effect of support groups, community nursing, TB clubs and home visits. Six of the studies concluded that the intervention reduced TB stigma while one instead found that stigma increased. The quality assessment of evidence indicated few rigorous evaluations and no study was found targeting enacted stigma.

Conclusion: Despite the dearth of rigorously evaluated intervention studies, the existing evidence suggests that knowledge shaping, community- and individual straightening interventions can be effective in reducing TB stigma. Several studies pointed at TB clubs that reduced both internalized and anticipated stigma. Our findings urge for future rigorous evaluations of interventions aimed at reducing stigma, as well as using measurement tools validated especially for this purpose.

A patient's tale

I Oxley,^{1,2} P Tisile¹ ¹TB PROOF, Cape Town, ²Nelson Mandela Metropolitan University, Dietetics, Port Elizabeth, South Africa. e-mail: ingridoxley@gmail.com

Phumeza Tisile was diagnosed with TB in 2010 while all along she had XDR-TB. The treatment of MDR-TB left her deaf in both ears. However she was told that she had pre-XDR-TB and her daily medication was increased with even more side effects. In 2011 she was discharged from Brooklyn Hospital to continue her treatment at home. Four months later they saw that the pre-XDR-TB drugs have stopped working, and she was diagnosed with XDR-TB. In August 2013 she was cured from XDR-TB but was left deaf. In 2015 February she got a once in a lifetime chance to hear again. She can hear now using cochlear implants. Tisile has done numerous advocacy works. She has presented the first Drug Resistant TB Manifesto at the 67th World Health Assembly in Geneva, which she co-authored. She did a plenary speech at the 46th Union World Conference on Lung Health. She has advocated at the Council for Scientific & Industrial Research (CSIR) seminar in TB infection control. In 2014 Tisile was awarded the Mail & Guardian young 200 in the category: Health-DR-TB activist.

Ingrid Oxley worked in a public hospital when she contracted pulmonary TB in 2011. She completed 9 months of TB treatment and was diagnosed with pre-XDR-TB in 2012. Both diagnoses of TB happened one month after being treated with immune suppressants for ulcerative colitis. During 2012, she was hospitalised for 75 days, of which she spent about one month in ICU as she developed liver failure from the TB medication and went into a coma. She miraculously recovered. Despite having social support from her family and friends and financial resources for health care, Ingrid found coping with daily tasks extremely difficult. After completing 24 months of TB treatment, she was cured and her quality of life drastically improved.

Ingrid and Phumeza are part of TB Proof, an NGO with the vision to break down the stigma attached to TB, educate the public about TB to promote early TB testing among symptomatic persons, and play an active role in addressing TB as a public health threat in South Africa.

SYMPOSIA: SATURDAY 29 OCTOBER 2016

40. TB elimination initiative in countries of the Latin American Region

Moving forward from TB control to TB elimination in Latin America Region

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In 1999 the National TB Programs of Chile, Costa Rica, Cuba and Uruguay, with technical assistance from PAHO/WHO, constituted the group of low TB incidence countries of Latin America (LA). These are the countries that reported incidence rates close to 20 cases per 100 000 population in the previous 5 years. They also achieved TB programmatic indicators according to international standards and have had robust surveillance systems for at least the 5 previous years. In successive meetings through the years, these countries defined steps and goals towards eliminating TB as a public health problem and began implementing plans with components related to: obtaining political commitment; strengthening laboratory networks, surveillance systems; TB control focus in vulnerable populations; the latent TB infection (LTBI) in contacts; training health workers; introducing TB in the agenda of academic institutions; infection control in health facilities; and engaging public and private providers in TB control as well as the community and civil society. In 2004, Canada, the United States and Puerto Rico were invited to join the group to enrich the exchange of experiences among the countries. In 2014, this group adopted the 'Framework towards TB elimination in low-incidence countries' as its own incorporating the eight priority actions for TB elimination tailored to their realities, the 'End TB Strategy' and the milestones and targets for 2030 and 2035. The countries are now strengthening what is already ongoing; implementing what is needed, especially with a greater focus on the vulnerable populations, LTBI and addressing TB social determinants.

Reference

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Addressing the TB elimination issue in Cuba

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A nationwide universally covered TB program has been implemented in Cuba since 1964. So far TB incidence reported in 2015 reached 6.2 cases per 100 000 population. The cure rate was 82% and TB-MDR keeps around 0.9%. Innovative actions are ongoing by systematic screening of vulnerable population groups (TB contacts, HIV infected, prisoners/ex-prisoners, students coming from TB high burden countries, and health care workers). Eligible people with latent TB infection receive preventive therapy. New investments on education-training, equipment, anti-TB drugs, new diagnostic and preventive tools are being gradually introduced. Process and impact indicators will be monitored and evaluated

41. It's time to scale up treatment of TB infection in high TB burden countries

Efficacy of rifamycin-based TB preventive therapy and experience of using 3HP in low burden countries

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This presentation will describe the evidence that rifamycin-based regimens are as efficacious as standard regimens in preventing TB in high-risk persons, current WHO Policy, and lessons learnt from scaling up 3HP in a low burden country.

Preventive therapy in children: policies, practice, performance, and perceptions

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This presentation will review current recommendations for preventive therapy in children, current practice in high and low burden settings, and discuss results from a knowledge, attitude, and perceptions (KAP) study of healthcare providers and parents in South Africa regarding isoniazid preventive therapy initiation for children under age 5 to better understand resistance to its uptake.

Novel rifamycin-based TB preventive therapy regimens and strategies for high burden settings

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This presentation will discuss the efficacy of rifamycin-based TB preventive therapy regimens in high burden

settings and describe novel strategies to further shorten the regimen and maximize the durability of TB preventive therapy

Lessons from the field: experience of scaling up 3HP in Pakistan

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Background: People exposed at home to TB face high risks of disease. TB infection treatment prevents progression to TB disease and death. The most efficient use of TB infection treatment is in the context of household contact investigations, allowing for early identification of disease and to benefit from TB infection treatment. We assessed the feasibility of screening drug-resistant (DR) TB household contacts for enrollment on infection treatment, as an extension to DR-TB program.

Methods: From May 2016, trained community health workers screened all household contacts of DR-TB patients enrolled at The Indus Hospital. Screening consisted of verbal symptom screen followed by a visit to the health facility for clinical and laboratory workup. Subjects diagnosed with TB disease were enrolled in TB disease treatment as per the national guidelines. Among those without TB disease, the following groups were eligible for and offered infection treatment: 1) younger than 5 years, 2) between 5 and 17 years with either a positive MT test or an immunosuppressive condition, or 3) 18 years and older with an immunosuppressive condition. All eligible subjects were consented and counseled before starting infection treatment of levofloxacin with either ethambutol or ethionamide for 6 months under DOT. All tests were offered free of cost and a transport allowance of USD 6 was provided to visit the facility for baseline workup. Subjects were followed at home and at clinic monthly.

Results: To date, we identified 35 eligible households; 28 were approached and all consented to participate. In these 28 households, 212 individuals were enumerated, of which 147 were approached and 146 consented and were verbally screened. Of these, 86 had clinical and laboratory investigations and one was found to have TB disease and started on treatment. Of the 28 subjects eligible to start infection treatment, 22 initiated treatment; 12 (55%) were females, 10 (45%) were < 5 years old, 6 (27%) were 5–17 years old, and 4 (18%) were ≥ 18 years old.

Conclusion: Screening of household contacts and enrollment on TB infection treatment was feasible in the setting of an established DR TB program, as an extension of routine contact investigation activities.

Pharmacokinetic aspects of 3HP regimen in special populations

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Scaling up of rifamycin-based TB preventive therapy will require administering the regimen to HIV-infected persons on antiretroviral therapy and pregnant women.

42. Reaching under-served groups to eliminate tuberculosis in England: patient perspectives, technological advances, and the role of the multi-disciplinary team

The epidemiology of TB in north-west England and its relationship with poverty

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Poverty and TB remain inextricably linked in north-west England. Whilst the majority of the global TB burden is in low-resource settings, being poor in high-resource settings remains a major risk factor for the development of TB and for adverse TB treatment outcomes. Evidence examining this relationship in England is scarce. This presentation will give an overview of TB epidemiology and the historical and future interventions to control TB in north-west England - the region in which this 47th Union conference is taking place. In addition, the presentation will explore the relationship between poverty and TB in north-west England and disseminate the findings of an analysis of the effects of socioeconomic status on TB outcomes and access to services. Finally, it will elaborate on the model of TB care in the north west and how that model aims to reach under-served, impoverished communities in north-west England.

The role of whole genome sequencing in detecting and reducing onward transmission of TB in England

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There have been many recent advances in TB diagnostic technology. Nucleic acid amplification and polymerase chain reaction techniques have provided rapid diagnosis and initial resistance profile. Newer molecular tests including whole genome sequencing (WGS) may allow detection of clustered TB cases. Funding has been mobilised to test all positive TB samples in England by WGS but its role in characterising TB clusters and influencing TB strategy is still in its infancy. Thus far in England, WGS has been shown to identify TB transmission not previously identified by traditional TB contact tracing. WGS analyses have also suggested that most

clustered TB cases occur in UK-born underserved groups including the homeless or drug-dependent. This presentation will elaborate on how WGS may be combined with traditional contact tracing to better characterise the epidemiology of TB in the UK and improved, targeted TB care for under-served groups to avoid onward TB transmission.

The role of the multi-disciplinary team and TB cohort review in reaching under-served groups

J Walker¹ ¹Liverpool University, Liverpool, UK. e-mail: jennifer.walker@liverpool.ac.uk

Under-served communities in England include those with drug and alcohol dependence, the formerly/currently incarcerated, migrants, and the homeless. Such vulnerable groups remain hard-to-reach through the current TB care model, despite England being a high-resource, low-prevalence setting. To eliminate TB, there is a need to implement novel multi-disciplinary approaches, including systematic TB cohort audit in collaboration with patient-groups and civil-society. This presentation, delivered by TB specialist nurses, describes the development and evaluation of the TB multi-disciplinary team in the north west of England, the largest geographical footprint in which TB cohort review has been undertaken. In addition, it will explore the role of TB cohort audit in identifying hard-to-reach TB patients and their household contacts and suggest ways in which to meet their health needs and improve their TB outcomes.

Patients' perceptions of barriers to accessing TB care and involvement of civil society in TB strategy

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Patient groups and civil society have often been overlooked when planning TB control strategies both globally and in England. Incorporating such organisations into planning and implementing TB policy would not only contribute to identifying perceived and actual barriers to accessing TB care but would strengthen TB control strategies. This presentation, given by a TB patient representative who has been centrally involved as a specialist committee member of the UK NICE TB Quality Standards Development Group, will expand upon the crucial role that patient groups and civil society can play in broadening the scope of the multi-disciplinary team. It will also elaborate the existing barriers that currently impede access to TB care in England, especially among under-served groups.

43. Novel quantitative approaches in paediatric tuberculosis

Childhood TB case fatality and implications for mortality estimates

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Background: Case fatality ratios among children with tuberculosis (TB) disease are poorly understood, particularly among HIV-infected cases and those not receiving tuberculosis treatment. Case fatality ratios could also offer an alternative source for estimating annual mortality in children with TB, currently estimated using vital registration data.

Methods: We carried out a systematic review of the published literature to identify studies of population-representative samples of pediatric (< 15 years old) TB cases. We used random effects meta-analysis to produce pooled estimates of case fatality ratios. We stratified our analyses by whether or not children received tuberculosis treatment, age (0–4 years, 5–14 years), and HIV status.

Findings: We identified 27 papers comprising 31 datasets representing 66,054 children with tuberculosis disease, of whom 9,038 died. Among children with tuberculosis from the pre-treatment era, the pooled case fatality ratio was 21.9% (95% confidence interval [CI] 18.1–26.4). The pooled case fatality ratio was significantly higher among children aged 0–4 years (43.6%; 95%CI 36.8–50.6) than among children aged 5–14 years (14.9%; 95%CI 11.5–19.1). In recent studies where the majority of children had tuberculosis treatment, the pooled case fatality ratio was 0.7% (95%CI 0.5–0.9). USA surveillance data suggest a substantially higher case fatality ratio among HIV-infected children receiving TB treatment, compared with HIV-uninfected children, especially without antiretroviral treatment.

Discussion: Without adequate treatment, children with tuberculosis disease, especially those under five years of age, are at high risk of death. HIV-infected children have an increased mortality risk, even when receiving tuberculosis treatment. Given that around two-thirds of the 1 million children that develop active tuberculosis each year are unlikely to receive treatment, our case fatality ratios indicate that mortality due to tuberculosis in children may be far higher than previously thought. In particular, tuberculosis should be considered one of the major causes of global under-five mortality.

Modelling to determine optimal dosing in treating paediatric TB meningitis

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This talk will describe the use of PK/PD modelling in optimising treatment dosing for children with TB meningitis

Modelling the cost-effectiveness of household contact screening for children

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This talk describes cost-effectiveness modelling of various household screening and preventive treatment strategies aimed at preventing TB in young children.

Host bio-signatures for TB diagnosis: analytical challenges and future directions

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This talk will discuss work analysing RNA expression with a view to developing diagnostics for TB in children.

The potential impact of BCG vaccine shortfalls on childhood mortality

R Harris,¹ PJ Dodd,² RG White¹

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Background: Bacillus Calmette-Guérin (BCG) vaccine is provided to over 100 million neonates annually to protect against childhood tuberculosis (TB). Recent BCG manufacturing interruptions highlight global supply risks. We estimated the potential impact of BCG shortfalls on global paediatric (< 15 years) tuberculosis mortality.

Methods: A static mathematical model was employed to estimate the number of paediatric TB deaths avoided by current BCG coverage, and potential additional TB deaths in the first 15 years of life due to one-year BCG supply shortfalls of 6.3% (as occurred in 2015) to 27.6% (as anticipated without mitigating action in 2015) assuming no catch-up campaigns.

Results: Preliminary results suggest that current BCG coverage was estimated to avoid 121,736 (95% uncertainty range (UR): 5031-325 482) TB deaths globally per birth cohort in the first 15 years of life. An estimated 12,174 (UR: 503-32 548) additional TB deaths would occur in the first 15 years of life per 10% (26 million dose) annual supply shortfall. A 16.5 million dose (6.3%) shortfall as reported at the close of 2015, reflecting 85% global coverage, was estimated as associated with 7726 (95% UR: 319-20 656) excess TB

deaths in the affected cohort in the first 15 years. A possible 25 892 (UR: 1070-69 227) additional deaths were avoided due to prompt shortfall reduction measures.

Conclusions: BCG shortages could greatly increase paediatric TB mortality. Although rapid action in 2015 minimised BCG shortfalls, avoiding a large number of potential additional deaths, the possible public health impact of even relatively small shortfalls highlights the critical importance of ensuring secure future manufacturing capacity and global BCG supply continuity.

44. Biosafety and tuberculosis infection control: sharing knowledge, challenges and solutions in TB laboratories

Overview of the risk assessment approach: story of implementation

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In 2012, WHO developed guidance based on assessment of the risks associated with different technical procedures performed in different types of TB laboratories. Risk assessments require careful judgement. On the one hand, underestimating risks may lead to laboratory staff being exposed to biological hazards. On the other hand, implementing more rigorous risk mitigation measures than are needed may result in an unnecessary burden on laboratory staff, higher costs to establish and maintain the laboratory's infrastructure, and an unsustainable situation. Risk assessments should consider the bacterial load of materials (such as specimens and cultures), the viability of the bacilli, whether the material handled is prone to generate aerosols during the activity being assessed, the laboratory's workload, the epidemiology of the disease, and the health of laboratory workers. Assessments should also consider other factors that may influence the likelihood or the consequence of exposure to TB.

Biosafety and infection control in TB laboratories: challenges and solutions

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Biosafety and infection control interventions are based on the risk of transmission. While a slightly different hierarchy of control is used for each, the rubrics are essentially the same. Challenges include understanding the risk of transmission, selection of measures to reduce the risk, and how to sustain those measures. Communication of the budget and capital needs to superiors is critical and communication to workers on how to ensure a healthy work environment are critical. This presentation will show some challenges that laboratories faced and the solutions that were applied.

Primary containment devices: their application, operation and maintenance

J Serle¹ ¹Germfree Laboratories, Inc., Ormond Beach, FL, USA. e-mail: jserle@germfree.com

Engineering controls play a critical role in laboratory biological safety and the prevention of laboratory acquired infections. Personal protective equipment (PPE), laboratory design features and primary containment devices are examples of common engineering controls. In particular, the proper use of primary containment devices can help the laboratorian safely handle infectious samples. This presentation will explore the different types of primary containment devices found in a TB laboratory and provide a fresh outlook on the operation and maintenance required to maintain safe microbiological practices.

Evolution of the TB laboratory in Vladimir Oblast, Russia

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The regional TB laboratory was originally located in the Vladimir TB Dispensary in the centre of Vladimir City. In 2002, the TB Dispensary was moved to an existing building in the outskirts of the City. A portion of the first floor was renovated to provide areas that met BSL 1, BSL 2, and BSL 3. As the diagnostic procedures and epidemiology of TB changed over the years, the diagnostic procedures and associated risk within the laboratory changed. The laboratory was renovated in 2015 in address the change in risk, change in equipment, and the aging infrastructure. This presentation will discuss the TB transmission risk assessments and decisions that went into each design as well as how the laboratory coped with change over time to provide in sustainable way both quality assured testing and safe working environment.

45. Adherence to confront resistance: social and behavioural interventions in Latin America

Peru: understanding social support mechanisms to influence health-seeking behaviour, resistance to treatment and overall patient well-being in TB patients

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This talk will identify aspects of health-seeking behaviour and strategies to positively influence this behaviour in order to improve tuberculosis treatment adherence and improved patient outcomes.

46. Low-level *M. tuberculosis* resistance: a challenge for the laboratory, an opportunity for MDR- and XDR-TB treatment

Redefining breakpoints for *M. tuberculosis* drug resistance

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Acquired drug resistance in *M. tuberculosis* is exclusively due to chromosomal alterations, such as mutations or deletions. Compared to all the genetic insight that has accumulated during the past years, little has changed in the laboratory procedures which define drug resistance for clinical *M. tuberculosis* isolates on the basis of critical concentration testing. Evidence is accumulating that drug resistance in *M. tuberculosis* is quite heterogeneous. Systematic genotype-phenotype studies have revealed that different SNPs are associated with quite distinct resistance levels. These findings indicate that established procedures for diagnostic drug susceptibility testing based on critical concentration testing have limitations and need to be complemented by quantitative measures of drug resistance.

Low-level fluoroquinolone resistance: an opportunity for improving XDR-TB treatment

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One of the major factors of poor prognosis of extensively drug resistant tuberculosis (XDR TB) is the resistance to fluoroquinolones (FQ). Genotypic and phenotypic studies have demonstrated that among *M. tuberculosis* FQ-resistant (FQ-R) strains, some are indeed resistant to older FQ such as ofloxacin (i.e. an MIC > 2 mg/L) but display only low-level resistance to newer FQ such as moxifloxacin (MXF) (i.e. an elevated MIC remaining below the usual pic serum level of MXF). Murine studies have shown that MXF retains some in vivo activity against FQ-R strains with MXF MICs below 2 mg/L. Such strains are mainly those harboring *gyrB* mutations but also some *gyrA* mutations such as D94A or to a less extent A90V. This concept has been confirmed clinically and thus supports the use of late generation FQ in case of extensively drug-resistant tuberculosis due to FQ-R strains with MXF MIC < 2 mg/L.

Detecting rifampicin low-level resistance: a challenge for the laboratory

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Background: Rifampicin resistance of TB bacilli is caused by mutations in the *rpoB* gene. Not all of those cause resistance, actually this effect seems to be restricted for over 95% to a short part of the gene, called the RRDR (rifampicin resistance-determining region). It spans codons 507 to 533 (*E. coli* numbering), but over half of rifampicin resistance mutations reported from systematic *rpoB* sequencing of retreatment cases is caused by 2 or 3 mutations in codons 526 and 531. These are characterized by a high level of resistance that is easily detected using conventional testing and parameters, such as the proportion method on LJ medium. However, the final original description of this method already mentions that low-level rifampicin resistance can also occur and requires testing at a second, lower critical concentration. With time, this has been ignored.

Methods: Proficiency testing for drug susceptibility tests (DST) among the supra-national TB laboratories showed highly unusual discordant results for rifampicin were obtained with some strains, carrying specific resistance mutations. We then determined prevalence and first-line treatment outcomes for systematic series of new or retreatment cases from different settings.

Results: While the prevalence of each low-level mutation may be only a few percent or less, together they represent 10-20% of all *rpoB* mutations in retreatment cases, provided sequencing is not restricted to a pre-selection of strains known to present resistance in conventional DST. For systematically tested new cases from Bangladesh, Hong-Kong and Pakistan, the proportion of low-resistance mutations among all those with a rifampicin-resistance mutation went from 20-50%. Moreover, in low-income settings the outcome of first-line regimens is as bad for low- as for high-level resistance.

Discussion: In the laboratory, this type of resistance is easily missed by phenotypic DST, particularly fast and automated methods such as MGIT, or even proportion method on LJ with final reading at four rather than six weeks. Lowering the critical concentration or incubating longer in general shows their resistance, but with a definite risk of false resistance appearing. Molecular DST seems to be the solution, provided an extended gold standard is accepted.

Bedaquiline low level resistance: risk factors and clinical impact

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Low level resistance to bedaquiline (BDQ) in clinical isolates is due to Resistance Associated Variants (RAVs) in Rv0678, a gene regulating the MmpS5-MmpL5 efflux system. Rv0678 RAVs were identified in some isolates from patients treated with BDQ, and led to moderate increases in MIC for both BDQ and clofazimine. The discovery of cross-resistance between BDQ and CFZ created some concern. Some clinicians assumed patients to be resistant to both BDQ and CFZ when Rv0678 mutations are identified. However, no clear relationship was observed between this low-level resistance to BDQ and treatment response (sputum culture conversion at endpoint). Recent data suggest that Rv0678 RAVs can often be identified in patients never exposed to BDQ or CFZ, and in most cases they are not associated with increased MICs for BDQ. The role of low trailing bedaquiline plasma levels in selecting Rv0678 RAVs will be discussed.

47. Modelling to overcome resistance to TB drugs and the End TB Strategy

Cost-effectiveness of triage testing for facility-based systematic screening for tuberculosis in Uganda

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Systematic screening has been proposed as one approach to help achieve the ambitious End TB Strategy goals, but the cost-effectiveness of systematic screening remains uncertain. We constructed a model of systematic screening for TB in a Ugandan clinic to evaluate the elements that would make systematic screening (by chest X-ray or point-of-care C-reactive protein) cost-effective in this setting. We describe the characteristics of both the population (e.g., underlying TB incidence) and the test (e.g., sensitivity, specificity, cost) that are necessary to make systematic screening for TB cost-effective in this context. These results may help guide decision-makers in implementing systematic screening strategies that are both cost-effective and impactful, as we seek to aggressively combat the TB epidemic in high-burden countries, and make progress towards the End TB Strategy goals.

Tradeoffs in new anti-tuberculosis drug introduction policies: a model based analysis

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Optimal strategies for introducing new TB drugs have not yet been established. We created a Markov decision model to follow a hypothetical cohort of MDR TB patients under different bedaquiline use strategies based on the resistance patterns of eligible patients. Both providing bedaquiline to all MDR patients and withholding it completely maximized the life expectancy of our initial cohort under some scenarios, reflecting assumed uncertainty in bedaquiline safety and efficacy. Liberal bedaquiline use strategies increased bedaquiline resistance, but decreased resistance to other MDR drugs. More liberal bedaquiline use strategies reduced the expected number of and life years lost to secondary cases. Continued research on bedaquiline is necessary to verify an overall mortality benefit in programmatic settings. Once established, the desire to prevent bedaquiline resistance by restricting its use should be weighed against the possibility of extending current patients' lives and protecting existing drugs through expanded use

Capturing in situ fitness costs of drug-resistant *Mycobacterium tuberculosis* in Peru

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The relative fitness of drug resistant *Mycobacterium tuberculosis* strains is a key determinant of their likely spread. In this project, we took data from a household study of the spread of *M. tuberculosis* in Lima, Peru and fitted a mathematical model to estimate the likely fitness of multidrug-resistant *M. tuberculosis* (MDR-TB) strains relative to the circulating sensitive strains. Our results suggest that the MDR-TB strains had a large fitness deficit. These results show how mathematical modelling can be used with in situ data to estimate important natural history parameters and will have important implications for the predictions of MDR-TB burden in the future

Understanding the contribution of social protection to accelerate TB elimination

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Social protection is a key pillar of the End TB strategy; however there is little direct empirical evidence to link this policy component to improved epidemiological outcomes. Evidence generation is hampered by funding limitations, ethical issues and the challenge of performing experimental research on governmental social protection programmes. Mathematical modelling can contribute to overcome these barriers by illustrating links

between indirect process data and population-level outcomes; however existing models are inadequate to encompass the complexity of socioeconomic phenomena. The S-PROTECT Modelling consortium is a multi-disciplinary team of experts aiming to develop an innovative mathematical modelling approach to better understand the role of social protection as a tool to facilitate the elimination of TB. We will present the first 10-months of S-PROTECT, including the theoretical framework, the methodological innovations, and how S-PROTECT and social protection will contribute to the End TB Strategy

Illness-related impoverishment averted by TB control: findings for India and South Africa

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One of the three targets for the End TB strategy is to eliminate catastrophic costs due to TB by 2020. The patient and household costs associated with the illness of tuberculosis (TB) can often be 'catastrophic,' a measurement of economic burden on households. We estimated the illness-related impoverishment averted by enhanced TB control in India and South Africa from 2016 to 2035, for three intervention strategies: 1) improved drug-susceptible (DS) TB care; 2) improved MDR-TB care; and 3) intensified case finding. We quantified intervention impact as changes in the number of households incurring catastrophic health costs, in line with WHO global targets. This will contribute to discussion on the potential contribution of these three interventions to the catastrophic costs target in the End TB strategy

48. Shortened regimens for the treatment of multidrug-resistant tuberculosis

The nine-month MDR-TB regimen: how does it work?

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Background: The 9-month regimen is the result of over ten years of development. At the start the intention was not a short regimen, but one that would be easy to apply in the field. It had to be standardized as the first-line regimens, as little toxic as possible by preferring re-use of

first-line drugs that might still be active over toxic second-line drugs, and relatively cheap to make it accessible for a maximum number of MDR-TB patients. It thus had to be highly effective without relying on individual drug susceptibility testing, using only aggregate resistance data.

Methods: It started as a long regimen close to WHO recommendations. Small cohorts were enrolled, resistance of the bacilli tested by a supra-national TB reference laboratory, and patients monitored closely until 2 years after end of treatment. This allowed to decide on small changes applied to the next cohort. Finally, after some five cohorts on ofloxacin-based regimens enrolled over 10 years, the total absence of relapse except in case of initial or acquired fluoroquinolone resistance suggested that a shorter regimen, based on the most active fluoroquinolones, moxi- or gatifloxacin, could be equally effective. This led to trying out the 9-month regimen.

Discussion: Gatifloxacin, the most powerful fluoroquinolone, is the 'core drug'. Besides a strong early killing effect, it has good sterilizing activity later on, thus preventing relapse. High dosing is preferred to kill also most of the often present resistant mutants. Kanamycin is a bactericidal companion drug, very useful to help eradicate the gatifloxacin resistant mutants. To avoid excess toxicity and resistance amplification to XDR, kanamycin is used for only four months, with extension to maximum 6 months. The strong sterilizing activity of clofazimine was shown in mice, and it also seems to protect against acquired fluoroquinolone resistance. With early detection avoiding repeated first-line regimens, pyrazinamide resistance will be rare, and its sterilising activity still sufficient to help prevent recurrences. High-dose isoniazid overcomes the MIC of most resistant TB bacilli, and seems to contribute to cure. Prothionamide and ethambutol are weak companion drugs, and may not be essential.

Results of the nine-month MDR-TB regimen in Bangladesh

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Of 814 patients treated for MDR TB until end of 2013, 707 proven MDR-TB patients received the standardized 9 month regimen. 107 patients were excluded due to no laboratory proof of MDR-TB or due to infection with non-tuberculous mycobacteria. Results are given for 707 patients: 589 (83.3%) success, 47 (6.7%) died, 55 (7.8%) lost to follow up and 16 (2.3%) failed treatment. Among 16 failure cases tested for fluoroquinolone resistance: 15 (94%) had high level fluoroquinolone resistance and 1 (6%) was susceptible. One of them was a primary XDR-TB. Out of 483 patients successfully treated and followed for 24 months, 5 (1%) relapsed: 3 had high level, 1 low level resistance and one sensitive to fluoroquinolone. Attempts were made to shorten the

length of kanamycin to 2 months to avoid hearing loss, but failure cases were 5 times higher.

Results of The Union's observational study of the nine-month MDR-TB regimen in Africa

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An observational study on the 9-month regimen (4KmGfxPtoHCfzEZ/5GfxCfzEZ) for multidrug-resistant tuberculosis (MDR-TB) was been set up in sub-Saharan countries in 2013. Adverse drug events, clinical and bacteriological response to treatment are followed up monthly until treatment completion, and bacteriological status is monitored 6-monthly thereafter for one year. We report the final results of this study from 8 French speaking countries (Benin, Burkina Faso, Burundi, Cameroon, Niger, Central African Republic, Democratic Republic of Congo and Rwanda), which included 878 patients: 36% females, 83% received previous TB treatment, 22% were HIV positive. The results are very similar to those of Bangladesh, with 81% success rate, 8% died, 8% lost to follow-up and 3% failures. Mild gastric pain and vomiting were frequent during the 2 first months. Hearing loss >70 dB was reported in 9.2% of the cohort. Severe adverse events were significantly more frequent among HIV-positive than HIV-negative patients.

Shorter and better? Results and challenges from of a simplified short regimen for multidrug-resistant tuberculosis in Karakalpakstan, Uzbekistan

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Standard multi-drug resistant tuberculosis (MDR-TB) treatment programmes report low success rates and significant adverse events. Médecins Sans Frontières (MSF) and the Uzbekistan Ministry of Health conducted a prospective single arm study of a modified short course 'Bangladesh' regimen treating patients without previous exposure to second line anti TB drugs. Between September 2013 and March 2015, 128 patients met inclusion and exclusion criteria. Culture conversion at 4 months was 85.6%. 92 (71.3%) patients successfully completed treatment, with 78% experiencing at least 1 adverse event. DAIDS grading, corrected QT interval changes and outcomes 1 year post treatment completion will be presented. Implications for scale up of the regimen will be discussed including patient selection in contexts with high second line drug resistance, adherence support for commencing ambulatory treatment from day 1, management of patients failing the regimen, and management of prolongation of corrected QT interval.

Scaling-up implementation of shortened MDR-TB regimens: what are the challenges?

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Treatment for multidrug-resistant tuberculosis is one of the hardest experiences for both patients and healthcare workers alike. Researchers and clinicians are called for a massive scale-up of programmatic management of MDR-TB mostly in resource-constrained settings. However several technical and operational barriers hinder the achievement of this scale-up. The shortened MDR-TB regimens are effective and inexpensive. They are indeed a step in the right direction for MDR-TB control. Published data from Bangladesh, Niger and Cameroon and preliminary results from an observational cohort study conducted by the Union in 9 African countries showed positive outcomes. The 9-month treatment option is significantly less burdensome for resource-limited settings than the standard WHO treatment of 20 months. We face up several challenges to scale-up shortened MDR-TB regimens: increase human resource capacity through the provision of standardized training for national staffs, ensure intensive treatment of adverse effects, promote ambulatory care and strengthen socioeconomic support for patients.

49. TB screening and isoniazid preventive therapy for pregnant and breastfeeding women in resource-limited settings

Maximising access to TB screening and isoniazid preventive therapy for pregnant and breastfeeding women

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TB is one of the top five killers of women and causes up to 34% of all maternal mortality when only indirect causes are considered. Maternal health services provide a vital opportunity for reducing morbidity and mortality from TB in both the mother and baby through the integration of TB services, including screening and TB preventive therapy. The World Health Organization is developing practical guidance, including training and monitoring and evaluation tools, to facilitate integration of TB and maternal health services in resource-limited settings. This presentation will highlight the needs and opportunities for TB and TB/HIV integration in maternal health services as well as promising practices for implementing integrated services.

Assessing the safety and effectiveness of isoniazid preventive therapy and antiretroviral treatment in HIV-infected pregnant women in high TB burden settings: IMPAACT P1078

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To date no trials of TB prevention in HIV-infected persons have included pregnant women. Given World Health Organization (WHO) recommendations to scale-up isoniazid preventive therapy (IPT) and antiretroviral treatment (ART) for all people living with HIV, additional data is needed about safety and efficacy during pregnancy and the postpartum period. Both ARVs and IPT have small but recognizable risk of hepatotoxicity. IMPAACT P1078 is a Phase IV double-blind placebo-controlled trial assessing the safety and efficacy of antepartum versus postpartum initiation of IPT in HIV-infected women who are receiving ART in 8 countries (Haiti, India, South Africa, Zimbabwe, Botswana, Uganda, Tanzania, Thailand). During this presentation, the study design, objectives, and baseline findings will be discussed.

Developing strategies for TB screening among HIV-infected and HIV-uninfected pregnant and postpartum women in Swaziland

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This presentation will describe findings from an operational research study to evaluate the sensitivity and specificity of the WHO TB screening tool for HIV-infected and HIV-uninfected pregnant and lactating women receiving antenatal and postnatal services in public health facilities in Swaziland. The study will also assess the value of enhanced screening algorithms, including additional symptoms and clinical/laboratory procedures and tests. This presentation will include discussion of preliminary clinical and laboratory analysis as well as describe operational considerations for TB screening in maternal and child health settings.

Evaluating the utility of the World Health Organization symptom screening algorithm for TB diagnosis among pregnant women in India

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Background: Pregnancy increases a woman's risk of developing tuberculosis (TB) and her likelihood to seek health care. We assessed a World Health Organization (WHO) recommended TB symptom screen in antenatal women in India.

Methods: This was a cross-sectional study of antenatal women at a government hospital in Pune, India. All HIV-positive women, and only those HIV-negative women with at least one symptom on the WHO TB screen (cough of any duration, fever, weight loss, night sweats) provided sputum samples, which were analyzed by direct sputum smear and GeneXpert. Sputum collection for the HIV-positive group was done by a different operator than that for the HIV-negative group.

Results: We enrolled 655 women. Median gestational age was 27 (IQR 20-33) weeks. Of 129 (19.7%) HIV-positive women, 115 (89%) were on antiretroviral therapy with a median CD4 count of 531 (IQR 381-709) cells/mm³. The symptom screen was positive in 142 (21.6%) women (29 HIV-positive, 113 HIV-negative.) On multivariate analysis controlling for HIV and contacts with night sweats, a positive symptom screen was associated with living in a rural area (OR 1.5, 95%CI 1.1-2.0, $P=0.006$.) Screening with sputum collection took a median of 15 minutes (IQR 13-20); without sputum collection took 8 minutes (IQR 6-10). Only 161 (66.5%) women asked to provide sputum were able to do so. On multivariate analysis, ability to provide sputum was associated with having a cough (OR 4.1, 95%CI 1.9-9.0, $P<0.005$), fever (OR 5.9, 95%CI 1.1-32, $P=0.039$), tobacco use (OR 3.8, 95%CI 1.1-12, $P=0.034$), and HIV (OR 8.9, 95%CI 4.2-19, $P<0.005$). Weight loss was associated with inability to provide sputum (OR 0.7, 95%CI 0.5-0.9, $P=0.013$). GeneXpert could not analyze 30 samples due to low volume. One case of active TB was detected in a HIV-positive participant with a positive symptom screen.

Conclusion: The utility of the WHO TB symptom screen is operator and symptom dependent. The screen was able to detect one case of active TB out of 129 HIV-positive women screened. Standardized training of the operators and a more focused screening tool may improve screening of pregnant women.

Performance of TST and QFT for LTBI screening during pregnancy and postpartum in HIV-infected Kenyan women

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Background: Immunologic changes in pregnancy and the postpartum period may affect latent TB infection (LTBI) diagnostic performance.

Methods: In our previously described study, we performed QFT and TST on 96 HIV-infected pregnant Kenya women, and repeated QFT/TST testing at 6 weeks postpartum in 86 women (excluding 10 QFT+/TST+ in

pregnancy). QFT identified more women with LTBI than TST in pregnancy (QFT 34.4% vs. TST 13.5%, $P=0.006$) and postpartum (QFT+ 29.5% vs. TST+ 14.1%, $P<0.0001$). For this analysis, test sensitivity was calculated using either positive test as a 'gold standard' of LTBI diagnosis and quantitative QFT mitogen and *M. tuberculosis* antigen (Mtb-Ag) IFN- γ responses were compared by peripartum stage.

Results: In pregnancy, QFT sensitivity to identify LTBI was higher than TST (91.7% vs. 36.1%, $P=0.0001$). Assuming 10 women initially QFT+/TST+ in pregnancy would have remained QFT+/TST+ postpartum, the sensitivity of QFT remained higher than TST postpartum (94.4% vs. 61.1%, $P=0.003$). However, TST sensitivity improved significantly (36.1% to 61.1%, $P=0.02$), while QFT sensitivity remained similar (91.7% vs. 94.4%, $P=0.26$). Of 86 women QFT-tested in pregnancy and postpartum, mean Mtb-Ag and mitogen IFN- γ response were lower in pregnancy vs. postpartum (Mtb-Ag: 1.03 vs. 1.54 IU/mL, $P=0.03$; mitogen: 4.46 vs. 7.64 IU/mL, $P<0.0001$). Among 22 QFT+ women in pregnancy and postpartum, mean Mtb-Ag IFN- γ response was lower in pregnancy than postpartum (3.46 vs 4.48 IU/mL, $P=0.007$). Ten QFT+/TST- pregnant women remained TST- postpartum, with lower Mtb-Ag IFN- γ response in pregnancy vs. postpartum (3.59 vs. 5.08 IU/mL, $P=0.09$). Eight QFT+/TST- women converted to TST+ postpartum, with non-significantly lower Mtb-Ag IFN- γ in pregnancy vs. postpartum (4.01 vs. 4.92 IU/mL, $P=0.19$). Most (41/44) QFT-/TST- pregnant women remained QFT-/TST- postpartum, without change in Mtb-Ag IFN- γ (0.04 vs. 0.04 IU/mL $P=0.93$). Of 3 with test conversion postpartum; 1 converted to QFT+/TST+ (Mtb-Ag IFN- γ increased from 0.03 to 8.07 IU/ml postpartum) and 2 converted to QFT+/TST- (mean Mtb-Ag IFN- γ increased from 0.0 to 2.33 IU/mL).

Conclusions: QFT had higher diagnostic sensitivity for LTBI detection than TST in pregnancy and postpartum. Lower QFT Mtb-Ag and mitogen IFN- γ responses in pregnancy than postpartum suggest pregnancy-associated immunologic changes may influence both QFT and TST test performance.

50. Trials of mice and men: recent advances and the future of TB drug development science

How critical is isoniazid?

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ACTG A5307 assessed the criticality of isoniazid in the early phase of TB treatment. In this EBA study, treatment with isoniazid for 2 days, for 14 days, for 2 days followed by 12 days of moxifloxacin and for 0 days was given alone with rifampin, PZA and ethambutol.

Optimised rifamycin and PZA doses derived from trials and models

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How clinical trial data and PK-PD modelling can help in finding the right doses for a drug, as demonstrated by the example of PZA and rifamycins.

Mouse tales and their predictions, building on the example of clofazimine

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Murine studies of TB drug efficacy are one of the most important tools for testing drugs and regimens in preclinical science. Their strengths and limitations will be discussed in the light of promising data on clofazimine.

Drug penetration into TB lesions - how does this add to rational drug development?

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Analyses of TB drug levels in actual TB lesions provide fascinating new insights into TB treatment. Recent advances are summarized and their inclusion into development of new drugs and regimens described. For successful treatment of tuberculosis, drugs must be carried from the blood compartment to poorly or non-vascularized lesion niches, reach adequate concentrations inside infected macrophages and other immune cells, and diffuse into the necrotic foci of granulomas and the caseum of cavities. We have measured and imaged the distribution of tuberculosis drugs and their active metabolites in various lesion types and lesion compartments, revealing very complex and heterogeneous penetration and diffusion patterns, which are both drug-specific and lesion-specific. We have also developed assays to determine the drug concentrations required to kill intralesional *M. tuberculosis*. Putting these datasets together, we better understand which drugs are likely to sterilize which lesion types, and use this information to propose combinations of drugs that complement each other in eliminating all bacterial populations on an infected lung. Finally, to inform medicinal chemistry campaigns, we have developed in vitro assays that predict penetration and diffusion properties within lesions. Our key objectives are to 1) optimize the use of existing TB drugs based on a pharmacological rationale, and 2) guide the design of new drug regimens taking into account the differential abilities of each companion drug to distribute into distinct lesion types, and combine drugs with complementary pharmacology.

Examples, learnings, better trials and regimens

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This talk will contain considerations around building an effective regimen and testing it in phase II, from a clinical trialist's point of view. Knowledge on TB and TB treatment is rapidly expanding, which challenges drug developers to use new methods wisely. Those methods include the necrotic granuloma mouse models, drug lesion concentrations, and increasing knowledge on drug tolerant phenotypes which are thought to play a key role in relapse. Pharmacokinetic regimen optimization holds promise to prevent new resistance, optimizing efficacy at minimal toxicity in the population, and choose the optimal dosing strategy as demonstrated for rifapentine. Companion diagnostics informing on individual drug metabolism might be a future tool. Improved trial designs for phase II can help in alleviating concerns over classical phase II endpoints that involve quantitative culture or culture conversion, and may use clinically relevant instead of surrogate outcomes for a decision to move a regimen to phase III, increasing accuracy of regimen selection.

51. TB and mental disorders: putting the science into practice

Mental health in MDR-TB management: an issue for patients, caregivers, and healthcare workers

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Individuals with MDR-TB have greater risk for comorbid depression, anxiety and psychosis stemming from the complexity and duration of MDR-TB treatment, amplified psychosocial stress, and complicated medication side-effects. This session will explore the challenges related to the co-management of TB and mental disorders and implications for patient care.

TB and mental health: a survey of national TB programme directors

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Background: Individuals with TB and mental or substance use disorders are more likely to delay seeking care, miss doses, default from treatment, develop drug resistance, fail treatment and/or die. They are also more likely to be infectious for longer periods, posing greater

risk for community transmission. Treating comorbid mental disorders among TB patients may help to curb the epidemic by improving health and mental health outcomes. The purpose of this study was to assess perceived needs, existing protocols, and receptivity to TB and mental health service integration in high burden countries.

Methods: We conducted 30 minute interviews with the National TB Program (NTP) Directors from nearly 20 high burden countries. The survey assessed the opinions of NTP directors about the current needs and protocols related to screening, referral and treatment of TB patients with co-morbid mental health and/or substance abuse issues. We also assessed receptivity to TB and mental health service integration by TB providers and at a national level.

Results: Whereas data collection is still underway, the most salient finding thus far has been that the majority expressed high receptivity to integrating mental health treatment into TB care to improve outcomes. The main barrier identified was limited human and material resources and low capacity to provide mental health treatment.

Conclusions: Several low-cost non-pharmaceutical mental health interventions exist that can be delivered by non-mental health specialists and have been effective in a range of low-resource settings. There is a critical need to adapt such interventions for integration into existing platforms of TB care and building the capacity of non-mental health specialists to effectively co-manage TB and mental illness.

Biomarkers for TB and depression

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Compelling evidence shows that elevated pro-inflammatory cytokines produced in response to other medical illnesses or treatments can trigger depression, even in individuals without a prior psychiatric history. This session will describe preliminary data exploring the association between TB, inflammation, and major depression.

TB and mental disorders in Bangladesh

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Background: Tuberculosis (TB) is a multi-systemic infectious disease caused by mycobacterium tuberculosis and is one of the leading causes of mortality in Bangladesh. Globally rates of mental illness of up to 70% have been identified in tuberculosis patients. According to World Health Organization's (WHO) estimate; Bangladesh is one of the high burden countries in the world. Every year more than 300 000 people develop this disease, and more than 80 000 patients die of it. Stigma often contributes to psychosocial problems and emotional suffering which may disturb patients' normal social lives, influence care seeking and affect

compliance with effective treatment. The study aimed to identify the TB related stigma and taboos in Bangladesh for effective TB control programme.

Methodology: The review explored the patterns of distress, socioeconomic and cultural context, perceived cause and care seeking behavior of TB patients using both qualitative and quantitative data.

Results: Women had higher level of stigma regarding non-disclosure, shamed or embarrassed, others think less of them, effect on others, others have avoided them, others refused to meet them, others think less of the family, problems for children, expected support from spouse, marital problem, problem for relative to marry, stay away from work and presumed other health problem. Men than women had high stigma in disclosed to confidant, problem to marry, spouse refuses sex, and decided to stay away.

Conclusions and recommendations: TB-related stigma burden in terms of psychosocial and emotional sufferings are usually greater among women. TB control programme ought to take appropriate measures to address the issues of stigma. Evaluation and management of mental disorders from tuberculosis patients may increase treatment compliance and reduce relapse and can improve the quality of life for patients with this chronic disease. Primary care health workers could screen the mental disorders symptoms in tuberculosis patients to counsel and guide them properly.

Co-managing psychiatric issues in patients undergoing treatment for MDR-TB in Peru

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This session will describe the co-management of psychiatric disorders among individuals with MDR-TB in Lima, Peru.

ABSTRACT PRESENTATIONS THURSDAY 27 OCTOBER 2016

e-POSTER SESSIONS

01. Child and adult MDR with modelling

EP-100-27 The global burden of drug-resistant tuberculosis in children: a mathematical model

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Background: Following infection, children are at increased risk of progression to tuberculosis (TB) disease; a condition that can be challenging to diagnose. New approaches to estimating the burden of TB in children have highlighted a shortfall in notifications, and suggest much larger burden of isoniazid-resistant and multidrug-resistant (MDR) disease than direct data indicate. No work has yet quantified the burden of infection with drug-resistant strains, considered other types of drug-resistance, or accounted for sampling uncertainty.

Methods: We extended a previously published mathematical model of TB in children and combined this with a new analysis of drug-resistance patterns to produce country-level, regional, and global estimates of drug-resistant infection and disease. We sampled the proportions with each drug resistance type from a Dirichlet-multinomial model using the absolute numbers of TB cases observed at a country-level with: isoniazid-monoresistance (HMR), rifampicin monoresistance, MDR, fluoroquinolone-resistant MDR, second-line injectable resistant MDR and MDR with resistance to both a fluoroquinolone and a second-line injectable (XDR). Where possible, we restricted to treatment-naïve cases and used these proportions as a proxy for those in children. When country-level data were absent, we resampled data from the first to be available from: the nearest 5 neighbour countries; the WHO epidemiological region; the world.

Results: Our analysis suggests that 850 000 children develop any form of TB each year with an incidence of 57 000 for HMR-TB, 25 000 for MDR-TB, and 1700 for XDR-TB. We estimate nearly 67 million children are infected with *M. tuberculosis*, 5 million of whom with HMR, 2 million with MDR, and 150 000 with XDR. Africa and South-East Asia regions dominate the overall contribution to TB in children, but WHO EMR, EUR and WPR regions are substantial contributors to the burden of drug-resistant TB due to their much higher proportions of resistance. Our estimates suggest that

MDR is now more common than HMR in the WHO EUR region.

Conclusions: Far more drug-resistant TB occurs in children than is diagnosed, and there is a large pool of drug-resistant infection. This has implications for approaches to empiric treatment and preventive therapy in some regions.

EP-101-27 Prognostic model for risk assessment of development of pre-XDR-TB (fluoroquinolone resistance) in patients with MDR-TB

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Background: Fluoroquinolones (FQ) are the most effective drugs in MDR-TB treatment. Development of *M. tuberculosis* resistance to FQ may reduce the clinical benefit of them. Prediction of acquired FQ-resistance (pre-XDR-FQ) development risk is important for prevention.

Objective: To develop a prognostic model (PM) for acquired pre-XDR-FQ risk assessment on the basis of previous research results.

Methods: Categorical and binary logistic regression methods were used for PM creation. Initially we performed a retrospective cohort study included 463 MDR-TB patients (115 with acquired pre-XDR-FQ, 348 without). As a result of univariate and multivariate analysis we evaluated medical, clinical, microbiological, socio-demographic factors associated with acquired FQ resistance risk increase. Statistically significant factors were included in the PM. All selected predictors and dependent variables (pre-XDR-FQ) were binary. Categorical regression analysis was performed using the CATREG procedure in SPSS. Analysis results are presented in the Figure. Calculated importance coefficients were multiplied by 100 and approximated to whole numbers. The score was assigned for each predictor. The total score was calculated for every cohort patient and logistic regression analysis was performed in which the predictor was the patients' total score and dependent variable was same.

Results: The regression equation $y = 0.055x - 2.964$ was obtained. It was used in the formula for the pre-XDR-FQ probability calculation. In addition we offered an interval estimation of the acquired pre-XDR-FQ development risk according to the patients' total score for practical use. Diagram may be used also.

Conclusion: A created PM may be used by TB-specialists for risk assessment of acquired pre-XDR-FQ development in patients with MDR-TB.

Figure 1. Categorical regression analysis results (the resulting table fragment)

Predictor	Standardized coefficients		F	Significance, p	Coefficient of the importance
	β	Bootstrap estimation (1000) of the standard error			
Combination of cavity lesions and dissemination	0,164	0,043	14,935	0,000	0,146
Growth of Mtb on solid media > 100 CFU	0,177	0,044	16,490	0,000	0,167
Initial drug resistance of Mtb to injectable aminoglycosides	0,149	0,041	13,385	0,000	0,072
Treatment interruptions	0,295	0,053	30,956	0,000	0,375
Reduction daily dose of FQ	0,136	0,053	6,655	0,010	0,047
Prescription of treatment regimens with inclusion less than 5 anti-TB drugs with saved sensitivity of Mtb	0,121	0,044	7,421	0,007	0,075
Use of resection surgery	-0,059	0,033	3,136	0,077	-0,029
Renal failure	0,088	0,047	3,498	0,062	0,028
Alcoholism or/and drug addiction	0,079	0,042	3,556	0,060	0,062

EP-102-27 Low-dose linezolid therapy attains putative pharmacokinetic/pharmacodynamic efficacy and toxicity targets in tuberculosis: meta-analysis and Monte Carlo simulation

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Background: Multi-drug resistant tuberculosis (MDR-TB) threatens to undermine global tuberculosis (TB) control; optimal antibiotic dosing is required to improve treatment. The oxazolidinone antibiotic linezolid is an important component of some MDR-TB regimens but must be administered for several months and the routine dose for gram-positive infections (600 mg BD) causes accumulative toxicity. Lower dosages may retain efficacy with less toxicity. Clinical pharmacokinetic/pharmacodynamic (PK/PD) studies are required to assess this approach as available data are limited.

Methods: Plasma PK/PD targets for efficacy (area under the concentration-time curve (AUC)_{0-24h}/minimum inhibitory concentration [MIC] >100h) and avoidance of toxicity (minimum concentration [C_{min}] < 2 µg/ml) for linezolid in TB therapy were established from published evidence. A systematic review and meta-analysis was performed to identify PK studies of TB patients receiving linezolid and produce summary estimates (with standard deviations; SDs) for AUC₀₋₂₄ and C_{min} at all doses. Combining these data (which were assumed to reflect underlying log-normal distributions) with known wild-type linezolid MIC distributions for TB, we performed Monte Carlo simulations, using R for Windows, version 3.2.2, to model what proportion of 100 000 individuals would attain our PK/PD targets at each dose.

Results: Six studies were suitable for meta-analysis, including linezolid doses of 300-600 mg OD or BD. Heterogeneity was low. Data was combined using a fixed effects model, allowing the estimation of a summary mean and SD for AUC₀₋₂₄ and C_{min} for all doses. During Monte Carlo simulation less than 0.1% of individuals failed to attain the AUC₀₋₂₄/MIC >100h efficacy target at every dose. At all but the highest (600mg BD) dose, >75% of simulated individuals attained the C_{min} < 2µg/ml toxicity avoidance target and at the lowest 300 mg OD dose, 97% attained the target.

Conclusions: At all doses of linezolid, including the lowest 300 mg OD dose, the efficacy target was satisfactorily attained. Whilst attainment of the toxicity avoidance target was highest for the 300 mg OD dose, high rates of attainment were also seen for all but the highest 600 mg BD dose. More data are needed to inform linezolid PK/PD targets in TB to determine optimal dosing strategies.

EP-103-27 Changing drug resistance profiles during tuberculosis treatment: amplification, apparent 'loss' of drug resistance, reinfection and mixed infection

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Background: Prior studies suggest that first-line therapy can select for a resistant subpopulation of *M. tuberculosis*, while poor adherence or second-line therapy can select for reemergence of drug-susceptible *M. tuberculosis* populations. The frequency of these events during tuberculosis (TB) treatment remains unclear. Here we quantify the changing resistance patterns and isolation of distinct *M. tuberculosis* strains during anti-tuberculosis treatment, within the context of a large prospective cohort study.

Methods: We enrolled patients with active TB in two health regions of Lima, Peru from September 2009 through August 2012. We obtained sputum for smear, culture, drug-susceptibility testing (DST), and 24-loci mycobacterial interspersed repeat unit-variable number tandem repeat (MIRU-VNTR) genotyping at baseline and at 2, 6 and 12 months after enrollment. We defined amplification of resistance as detection of new resistance in an isolate with a MIRU-VNTR signature identical to the baseline isolate, apparent 'loss' of drug resistance as susceptibility in an isolate with a MIRU-VNTR signature identical to the baseline isolate which was previously classified as resistant, reinfection as identification of an isolate with a different MIRU-VNTR signature than the

baseline isolate, and mixed infection as isolation of two or more isolates with different MIRU-VNTR signatures. **Results:** Four-hundred and three patients had more than one DST result available during tuberculosis treatment. Of these, 239 (59.3%) had no change in DST profile during treatment, 73 (18.1%) had a change in DST profile among isolates with identical MIRU-VNTR signatures, and 84 (20.8%) had a change in DST profile among isolates with different MIRU-VNTR signatures. **Conclusions:** We found that while most TB patients have durable DST profiles during treatment, about one-fifth have measurable differences in their DST profile among isolates with identical genotypic signatures which are attributable to either amplification of resistance or apparent 'loss' of drug resistance. Among those patients with a change in DST profile among isolates with different genotypic signatures, we distinguish between reinfection and mixed infection as the causative mechanisms.

EP-104-27 Latent tuberculosis infection and tuberculosis disease in paediatric contacts of drug-resistant tuberculosis patients in Armenia

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Background: Child contacts of adults with tuberculosis (TB) are more likely to become infected and have a higher risk of progressing rapidly to active TB disease compared to adult contacts. We measured prevalence and incidence of latent TB infection (LTBI) and TB disease in a cohort of DR-TB paediatric contacts in Armenia.

Methods: Prospective cohort study. Children aged below 15 years in regular contact with newly diagnosed DR-TB index case in Armenia were eligible for inclusion. Clinical exam, chest X-ray, TST and IGRA were performed at inclusion and during 12-month follow-up. LTBI was defined as TST ≥ 10 mm or positive IGRA test in asymptomatic contacts with a normal chest X-ray. A child with a decision of TB treatment was considered as having TB disease. No chemoprophylaxis was administered.

Results: From June 2012 to December 2014, 151 children who were in contact with 82 DR-TB index cases were included in the study. Mean age was 7 years and 55.6% were girls. At inclusion, LTBI was diagnosed in 94 children (62.3%, 95%CI 54.0-70.0) and TB disease in one child (0.7%, 95%CI 0.01-3.6). Of the 43 non-infected children followed during 12 months, 6 (14.0%) became infected. No additional child was diagnosed with TB disease. Incidence rate of LTBI was 13.0 (95%CI 4.9-34.5) new infections/100 person-years. The only factor associated with LTBI at 12 months was smear-positivity of the index case (OR = 5.31, 95%CI 2.54-11.09). The number of hours of contact with the index case and

sleeping in the same room were not associated with TB infection. Agreement between the TST and the IGRA test in detecting LTBI was fairly good (83.9% concordance, kappa = 0.66).

Conclusions: Despite the high proportion of LTBI in paediatric contacts of DR-TB patients and the absence of prophylaxis, there was only one case of TB disease. These findings do not support the indication of systematic DR-TB prophylaxis in infected paediatric contacts contrary to what has been suggested in other settings. Nevertheless, screening of child contacts of DR-TB patients is highly recommended and particular attention should be given to children in contact with smear-positive patients.

EP-105-27 High treatment success in children treated for multidrug-resistant tuberculosis in Kenya: a retrospective evaluation

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Background: Tuberculosis (TB) is a common cause of morbidity and mortality in children throughout the developing world. Unlike adults, children are less likely to acquire resistance during the treatment of TB due to lower bacillary load. And when they do, they are infected with strains from an adult with drug-resistant TB (DR TB). The objective of this evaluation was to describe the demographic and clinical characteristics, treatment outcome in children treated for MDR-TB in Kenya between 2008 and 2015.

Methods: We conducted a retrospective analysis of secondary electronic data of all children (< 15 years) treated for MDR-TB between January 2008 and December 2015. Each child received 20 to 24 months of therapy with standardized treatment regimen to which their *Mycobacterium tuberculosis* strain was presumed to be sensitive. The primary outcome was treatment success, defined as a composite of cure and treatment completion.

Results: We abstracted 44 records of paediatric cases with a median age of 13 years (IQR 11-14). The f:m sex ratio was 2:1 with 34 (84%) and 31 (71%) with smear and culture positive laboratory results, respectively. One child was clinically diagnosed with XDR-TB. The average sputum and culture conversion during treatment was at month 3 of treatment. HIV testing was 100% with a positivity rate of 34% (15) and 100% ART uptake. 38 (86%) had malnutrition of whom 18 (40%) with severe malnutrition, all were offered nutritional support. The TSR for the cases was 90% (19) with a mortality rate of 10% (2) for the 2008-2013 cohorts.

Conclusions: MDR-TB can be successfully treated and therapy well tolerated among children in resource-limited settings. There is a need to ensure that contact investigation for intensified case finding among children

is conducted so as ensure early diagnosis and treatment of paediatric MDR-TB .

EP-106-27 Pediatric drug-resistant TB case finding and treatment outcomes in a decentralized setting in the Eastern Cape

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Background: Pediatric DR-TB is grossly under-diagnosed. Children with DR-TB are mostly managed in central hospitals worldwide and spend prolonged periods away from their caregivers.

Methods: Hospital based outreach teams were established for contact tracing and screening of all infectious adult cases. The study period was over 12 months. At each home visit the team did symptom screening of all close contacts (focusing mainly on the under fives and HIV-positive children), sputum samples for older children, HIV testing and referral of all symptomatic children to the hospital for further tests. The asymptomatic under five children were placed on a 3 drug prophylaxis and those with DR-TB were started on the standard regimens. The majority of the children (especially aged over 5) were managed as outpatients. All children were followed up for 18-24 months.

Results: A total of 100 adult DR-TB cases were identified as index cases. 600 household contacts were screened, with children aged under 12 making up one third (200). One hundred children (50%) were DR-TB contacts. Asymptomatic under-fives totaled 5 (20%). Twenty (20%) children were diagnosed with DR-TB. Two of the children (10%) were HIV-positive. The age ranges of the children with DR-TB were 3 months to 11 years. Failure to thrive was the most common presentation with 10/20 (50%). Cough and wheeze were each present in 4/20 case (20%). The methods of diagnosis were sputum (8/20), IS (4/20), GA (2/20), FNAB (2/20) and clinical (4/20) cases. 15/20 (75%) were MDR-TB, 2/20 (10%) rifampicin monoresistant, 1/20 (5%) Pre-XDR and 2/20 (10%) XDR-TB. Adverse events were uncommon and mostly mild. Deafness and hypothyroidism were most common with 4/20 (20%) cases each. There was a 100% successful treatment outcome with 15/20 (75%) cured and 5/20 (25%) treatment completed. There was zero mortality in this pediatric cohort.

Conclusions: This study demonstrated the value of intensive contact tracing and screening of child contacts. There was a 20% incidence of DR-TB amongst this cohort. Although challenging, bacteriological confirmation is possible in up to 50% of children. Successful decentralized management of children is possible with the proper training, resources and the support of partners. Very high successful treatment outcomes are possible in children with DR-TB (as reported in other studies) with very few serious adverse events. We recommend that more primary health care nurses and doctors be capacitated in doing GA, IS and FNAB to diagnose more children with DR-TB. All TB hospitals

should establish similar outreach teams to increase case finding of pediatric DR-TB.

EP-107-27 Treatment effectiveness among new isoniazid-resistant tuberculosis cases in Latvia

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Background: Tuberculosis (TB) is a major public health problem in Latvia, with approximately 800 cases registered and an estimated TB incidence rate of 50 per 100 000 population per year. Isoniazid (H) mono and polyresistance is registered for 15% of culture positive cases during the last years. Treatment regimen for H-resistant TB cases is adjusted with one of fluorquinolons (FQ) with or without injectable kanamycin (KM) since 2008 in Latvia. The aim of his study was to assess treatment efficacy, treatment duration and outcomes for H-resistant TB cases.

Methods: A retrospective cohort study of pulmonary TB patients with any kind of H resistance excluding MDR registered from January 2011 to December 2013. Data were extracted from the National TB registry and medical records. Results were analysed by descriptive statistics tools.

Results: Of 324 of H-resistant cases, 27 were excluded from analysis due to missing information and 30 as retreatment cases. 267 new TB cases (79 (30%) females, 188 (70%) males) were analysed. The mean age was 42.7 years, 8.4% of patients also had extra-pulmonary TB; 10.1% were HIV positive. Resistance to H, streptomycin (S): 230 (85%) patients; to H S and ethambutol (E): 25 (9.4%); to H, S and pyrazinamide (Z): 11 (4.1%); to H, S and KM: 1 (1.5%) patient. FQ was added to the treatment regimen for 170 (63.8%) cases, injectable for 2 (0.7%) cases and both for 65 (24.3%) cases; no changes were made in 30 (11.2%) cases. Treatment regimen was adopted on average after 34 days (ranged from 1 to 133 days) after first-line treatment start based on drug sensitivity tests received on liquid or solid media. Treatment results: 217 (81.3%) cured and completed, 24 (7.4%) defaulted, 19 (7.1%) died, 12 (4.2%) transferred out. Mean duration of treatment was 7.25 months (range 3.6-19 months) for cured patients. After a 2 year follow up period, 260 (97.4%) of cases are relapse free.

Conclusions: With treatment adjustment according to drug sensitivity data, it is possible to achieve good treatment results with a high relapse-free rate after a 2 year follow-up period.

EP-108-27 Efficacy and tolerability of linezolid for the treatment of extensively drug-resistant tuberculosis in Latvia

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Background: Despite the overall success in programmatic management of drug resistant TB, the growing proportion of XDR-TB poses a great challenge to the multidrug resistant (MDR-TB) control program in Latvia. From 2000-2014 the XDR-TB proportion increased from 2% (4 of 200 cases) to 15% (10/69 cases) with the treatment success rate of 50% using the standard MDR-TB treatment regimen. Starting from 2009, linezolid (LZD) became available for XDR-TB treatment in Latvia.¹

Methods: A retrospective cohort study to evaluate the treatment efficacy and safety of XDR-TB treatment regimens containing LZD during January 2009-December 2014. Data were obtained from patients' medical records.

Results: During the study period 42 XDR-TB patients (33 (79%) males and 9 (21%) females) received LZD. 15 (36%) patients were previously treated for TB; 7 patients were HIV positive. For all patients LZD was given as 600 mg daily after the initial dose of 1200 mg daily during the first month of treatment. The average time of total XDR-TB treatment duration was 21.9 months with 14 months (range 4-22) of average use of LZD. LZD was discontinued for one (2% of 42 cases) of 2 patients who developed symptoms of polyneuropathy. Comparing the total count of erythrocytes, hemoglobin and platelets at the beginning of treatment and at the end, for 29, 32 and 37 patients, respectively, these levels were decreased at the end of treatment which were diagnosed due to close follow up and did not lead to discontinuation of LZD treatment. Treatment results: 83% cured, 7% treatment failure, 5% died, 5% lost to follow-up.

Conclusions: Our experience demonstrates acceptable tolerability of LZD even during long term use with only 2% of cases discontinuing the drug due to side effects. LZD could be used for more than 12 months, but close monitoring of possible hematological and neurological side effects is essential.

Reference

1 Kukša L, Riekstina V, Leimane V, et al. Multi- and extensively drug-resistant tuberculosis in Latvia: trends, characteristics and treatment outcomes. *Public Health Action* 2014; 43: S47-S53.

EP-109-27 Reducing wastage of second-line anti-tuberculosis medicines at the end of the supply chain: experience of the Lesotho MDR-TB Program

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Background and challenges to implementation: Partners in Health Lesotho launched a community based MDR-TB treatment program in 2007 and more than 1300 patients have been enrolled since then. Second line and ancillary medicines are initiated by experienced clinicians and DOT is administered by trained treatment supporters. The centrally based pharmacy dispatches prescribed medication to each patient on a monthly basis. A thermal bag is used for the transportation and storage of medicines at patients' homes to maintain quality. Once the dispatch is made, medicines and other health commodities might be left over on the patient side due to:

- 1 Dose adjustment because of side effects and laboratory results
- 2 The whole treatment might be discontinued due to adverse drug reactions
- 3 Patients are given 30 days treatment for all drugs but the visit is every 28 days

As a result significant amounts of medicines are left unused and these might not be documented or accounted for.

Intervention or response: Second line anti-tuberculosis medicines (in strip, blister, sachet package and injectable formulation), which were kept in the thermal bags, were collected back to the pharmacy in cases where they were not used after each visit. Each item was checked for package integrity, expiry date and captured in the electronic system so that they could be re-dispensed.

Results and lessons learnt: From June 2015 to February 2016, almost all second line medications with a total cost of US \$43 432.33 were captured in the electronic system as a left over from patients and were re-dispensed. This is nearly a cost of a full treatment regimen for 10 patients considering the cheapest MDR-TB regimen. Para-aminosalicylic acid sodium, capreomycin and kanamycin accounted for 50%, 20% and 19%, respectively.

Conclusions and key recommendations: Regular accounting of leftover second -line TB medicines at the end side of the supply chain helps save money. National TB programs should track dispensed medicines, where applicable, to the last pill to minimize wastage. Based on this experience, we recommended programs to use blister or stripe packaging and thermal bags to help recover uncontaminated medicines from the patient side and protect medicines from degradation.

02. From screening and integration to outcomes

EP-110-27 Risk of tuberculosis among HIV seropositive persons: a meta-analysis of longitudinal studies from 1983 to 2015

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Background: HIV confers the greatest known risk for tuberculosis (TB) because of its detrimental effect on host cellular immunity. The risk of developing active TB, however, in HIV-infected persons may vary across populations because it depends on the level of immunosuppression, treatment of either HIV or TB, and other epidemiological or social factors.

Methods: To estimate the incidence rate of TB in HIV-infected individuals and understand its variability, we performed a meta-analysis of 109 longitudinal studies: 91 (83%) cohort studies and 18 (17%) clinical trials of TB incidence published between 1983 and 2015. The studies comprised 273 unique cohorts and 498 392 HIV sero-positive individuals from 5 continents. Data was extracted on the following clinical characteristics; tuberculin skin test (TST) status, isoniazid preventive therapy (IPT), CD4 status, and combination antiretroviral therapy (cART). The cohort, not the study was the unit of analysis, as many studies contained outcome data from more than one type of cohort.

Results: Among all cohorts, the overall incidence of TB was 1.66 cases/100 person-years (95%CI 1.42-1.95) with a high degree of heterogeneity ($I^2 = 99.5\%$). When stratified by TST and IPT status, the pooled TB incidence was highest in cohorts with untreated latent TB infection (5.5 cases/100 person-years). When stratified by CD4 and cART status, TB incidence was highest in cohorts with CD4+ T-cell counts < 200 cells/mm³ who did not receive cART (5.14 cases/100 person-years). TB incidence was lowest in cohorts with preserved immunity. There was substantial variability in TB incidence rates that was partially explained by gross domestic product (45%), level of immunosuppression (9%), and treatment effects (6%).

Conclusions: We found that the incidence of TB in HIV infection was highest in cohorts with untreated LTBI and in those with CD4+ T-cells < 200 cells/mm³. TB incidence depended largely on the extent of immunosuppression, at the individual level, and the standard of living, at the population level. While treatment of both latent tuberculosis infection and HIV infection reduce incidence of tuberculosis, external factors relating to poverty or allocation of resources toward public health and development may have a greater effect on TB incidence.

EP-111-27 Psycho-social support to children and adolescents with HIV and infected with tuberculosis: a forgotten crucial element for TB-HIV treatment adherence

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Background and challenges to implementation: PASADA is a faith-based organization that works in the HIV field since 1992. Its integrated TB/HIV program started in 2003 and is collaborating with partners including the Norwegian Heart and Lung Patient organization on TB/HIV service provision. One area of interest is patient-empowerment and psycho-social support to children living with HIV and co-infected with TB. Children and adolescents living with HIV and co-infected with TB face challenges of the diseases themselves, disclosure and treatment adherence. These could result in the development of drug resistance hence poor prognosis.

Intervention or response: A 5 day session for children and adolescents living with HIV and co-infected with TB was conducted. Facilitators were from a multidisciplinary team including medical professionals, social-workers and community volunteers. The aim was to provide a holistic management package for children and adolescent health. Topics covered included the relationship between HIV and TB, child's rights perspectives, protection from harm, dignity and respect, trust and stability, gender sensitivity, forgiveness/letting go and culturally appropriate psycho-social services. Teaching methods were discussion, group work, brainstorming, story-telling and playing therapy.

Results and lessons learnt: Three groups of 16 children and adolescents aged 10-16 years participated in the sessions (28 females and 20 males). They knew their potential in their families, accepted the fact that they live with HIV and are co-infected with TB and will get cured from TB; they forgave their parents for infecting them, and forgave those who didn't disclose to them their status. They made an appeal to each other on doing best to achieve life goals and to seek assistance from legal systems whenever they have problems. This intervention has had a very significant impact on the children and adolescents who were involved. Forty five per cent (45%) were reluctant to take their ARVs and anti-tuberculosis medicines willingly. After these sessions, all of them became 100% adherent to all medications.

Conclusions and key recommendations: Children and adolescents have underlying issues which affect their adherence and therefore need to be discussed and understood. Psycho-social support for children and adolescents needs to be introduced in TB/HIV programs to improve treatment adherence and reduce loss to follow-up and resistance to treatments.

EP-113-27 Improving ART access in TB services in selected facilities in South Africa

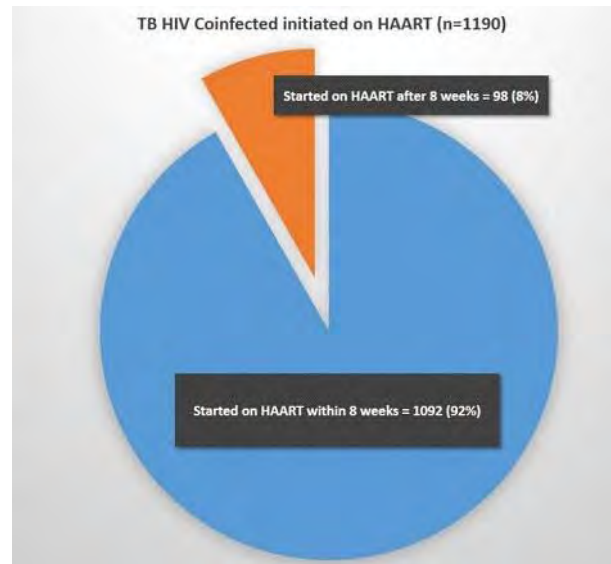
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Background: The South Africa (SA) guidelines recommend antiretroviral therapy (ART) initiation within eight weeks of starting tuberculosis (TB) treatment, regardless of CD4+ count to increase survival among people living with HIV. To increase access to ARVs at primary health care (PHC) level, nurses were trained to prescribe ARVs within the nurse initiated and managed antiretroviral therapy (NIMART) programme. The USAID TB Care II SA project supported the Department of Health in strengthening integration of TB and HIV services by training health care workers, including NIMART trained nurses. In addition, the project advocated for these nurses to manage or to have oversight of TB care services, where possible.

Methods: ART access of the TB/HIV co-infected patients in USAID TB CARE II-supported facilities was assessed. A data collection tool was developed and tested. We selected 55 facilities and assessed TB patient records who were enrolled on TB treatment between January and June 2015. We included TB patients who had also HIV co-infection, but were not initiated on ART.

Results: In the 55 facilities, we identified 1290 clinical records of TB HIV co-infected patients who were not on HAART prior to TB treatment. Analysis showed, that 1190 patients (92%) were initiated on HAART at any time during TB treatment. Of the 1190 patients, 1092 (92%) started ART within eight weeks of TB treatment initiation, as per the South African TB and HIV guidelines. The Figure below shows the details.

Conclusions: Training of NIMART nurses on TB management and advocating for them to have oversight on the care for TB patients led to more TB/HIV co-infected patients being initiated on HAART, with most starting ART as per national guidelines. This model should be advocated in other PHC facilities to strengthen TB/HIV integration and improve treatment outcomes.



EP-114-27 Optimizing the detection of TB among key populations using the Xpert® MTB/RIF assay in Northwest Cameroon

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Background: The Northwest region of Cameroon has a high HIV prevalence relative to the national average (6.3% vs. 4.3% of people living with HIV) and also a higher rate of HIV among people with TB (60% co-infection vs. 38% nationally; 2014 NTP data). To improve detection of TB in key populations, intensified case finding was introduced at 11 health facilities in the region, and the Xpert® MTB/RIF assay was implemented as the initial test for diagnosis of TB in people living with HIV. These activities were implemented with funds provided by the Stop TB Partnership's TB REACH initiative.

Methods: Intensified case finding was implemented by staff at health facilities in the region, including upfront Xpert MTB/RIF testing for people falling into one of four intervention categories, as shown below. Seven GeneXpert® systems were installed at hospitals, and an eighth system was already in place and was used as the central node of a sputum transportation network of 4 additional sites.

Results: Over 1 year, a total of 12 752 Xpert MTB/RIF tests were performed among the target population at the 11 main project sites. A summary of the percentage of those tested who were positive for TB and the number needed to screen to identify one TB case are shown by intervention in the Table. This combination of intensified case finding and upfront Xpert MTB/RIF testing led to improvements in TB case detection; during the year in

which these activities were implemented, the number of people tested in the labs increased by > 80% and the number of people with bacteriologically-confirmed TB diagnosed in the lab increased by > 40%, as compared to the year before these activities were started.

Conclusions: These activities resulted in improved TB detection and linkage to appropriate treatment for key populations. Further evaluation of population level impact is underway for these ongoing activities.

Table Number tested, % positive and NNS by intervention

	Intervention 1- Prior to antiretroviral (ART) initiation	Intervention 2- Hospitalized patients with symptoms of TB and/or known to be living with HIV	Intervention 3- HIV+ outpatients presenting at health facilities with symptom(s) of TB	Intervention 4- Others at high risk identified by lab or clinicians
Number tested	2659	3141	3407	3544
% positive for TB	7.1%	12.3%	5.0%	9.9%
Number needed to screen (NNS)	14	8	20	10

EP-115-27 Assessment of intensified case finding and isoniazid preventive therapy at health facilities providing HIV care and treatment services in Namibia

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Background: To reduce the burden of tuberculosis (TB) among people living with HIV (PLHIV), the World Health Organization, (WHO) recommends intensified TB case finding (ICF) among PLHIV and provision of isoniazid preventative therapy (IPT) to all eligible PLHIV. Namibian guidelines have included these recommendations since 2005, but the extent of implementation is unknown.

Methods: This study aimed to assess TB screening and provision of IPT among PLHIV in Namibia. HIV care and treatment facilities were selected based on facility type, size, and geography. PLHIV receiving HIV care and treatment during July-September 2013 were sampled proportional to facility size. HIV patient care booklets were reviewed to collect clinical HIV information as well as TB screening and IPT information. Patients with any documentation of screening or IPT were then matched against the relevant TB registers (e.g., sputum, TB treatment, and IPT). The implementation of ICF and IPT was analyzed descriptively by facility and patient characteristics.

Results: Of 859 sampled patients, 697 (81.4%) were screened for TB and 114 (16.3%) were referred for TB testing. Among 664 IPT eligible patients (defined as those screened negative for active TB disease), 299 (45.0%) were initiated on IPT. Only 58.6% ($n = 121$, unadjusted 95%CI 50.6%-66.1%) of pre-ART patients received TB screening compared to 91.3% ($n = 526$, unadjusted 95%CI 88.8-93.4) of patients on ART. Among patients receiving HIV care at a hospital, 352 (85.4%) were screened and 188 (45.2%) eligible patients initiated IPT. TB screening and IPT initiation and completion varied by district. IPT uptake was poor among women (38.1%) and children aged less than 14 years (28.6%). Total IPT completion among those who initiated preventive treatment was 152 (50.8%).

Conclusions: To reduce TB among PLHIV in Namibia, additional efforts are needed to ensure that all PLHIV are screened for TB and that those eligible receive and complete IPT. It is recommended to prioritize these services in low-performing areas and ensure the inclusion of missed populations including pre-ART patients, women, and certain age groups.

EP-116-27 Integration of TB and AIDS case management for migrants using the Reach-Recruit-Test-Treat and Retain (RRTTR) strategy

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Background and challenges to implementation: Non-Thai migrants who come to Thailand to work and live may be at risk of infectious disease and should receive prevention, care and treatment just as other Thais, especially now in the era of the ASEAN Economic Community when more cross-border migration is anticipated. The GFATM, through its new funding model, has provided a grant to World Vision Foundation of Thailand (WVFT) to implement a project in six higher-prevalence provinces of Thailand (Tak, Kanchanaburi, Bangkok, Pathumthani, Ranong, and Phuket) to prevent TB and HIV among migrants from Myanmar, Cambodia and Lao PDR through a Reach-Recruit-Test-Treat and Retain strategy.

Intervention or response: The project uses migrant health volunteers (MHV) to conduct outreach education, condom distribution and referral for migrants in need. Migrants diagnosed with TB or HIV are assigned a 'buddy' to ensure treatment compliance. The project uses a screening questionnaire to identify migrants who might have risk for TB or HIV. The project serves all vulnerable migrants, regardless of whether they entered Thailand legally or not. WVFT assists migrants with TB or HIV to return to their homeland to receive on-going care.

Results and lessons learnt: In 2015, the project was able to convene over 50 advocacy meetings with GOs/NGOs, recruit and train 556 MHVs, link 12 915 migrants with TB-HIV services, open six migrant drop-in centers, distribute 239 679 condoms, link 2402 migrants with HIV counselling and testing (and, knowing the results),

refer 60 PLWHA for care (with 23 migrants receiving ART), notify and register all migrants diagnosed with TB (127 cases), and conduct 114 home visits. Despite these accomplishments, there remain challenges to working with migrants and helping them access care in the Thai health system, especially those who entered Thailand illegally. There needs to be clarification of the referral system for migrants, both those in Thailand legally and undocumented migrants

Conclusions and key recommendations: There also need to be mechanisms to continue project interventions after external funding ends in 2016. Without these on-going interventions, Thailand may have difficulty achieving its public health goals.

EP-117-27 Tuberculosis treatment success among HIV-infected persons: a retrospective comparison of rural and urban care practices in western and central Uganda

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Background: Uganda is a sub-Saharan African country with both high incidence of TB (161 cases per 100 000 population in 2013) and high prevalence of HIV infection (7.3% among 15-49 year olds in 2011). TB treatment success rates have greatly improved in Uganda since 1995, getting closer to the World Assembly target of treating 85% of acid-fast bacilli smear-positive TB patients. A treatment success rate of 73% was reported among HIV-positive TB cases in 2013. However, rural based health care providers still report lower rates compared to national rates. This study aimed to investigate the current TB treatment success in rural and urban care providers, and examine modifiable factors that could be applied in rural settings to increase treatment success.

Methods: TB treatment success was defined as a sum of patients cured or completed treatment after TB treatment initiation. Data were obtained from six urban and 20 of 44 rural Ministry of Health - Infectious Diseases Institute collaborating clinics. People aged ≥ 14 years living with HIV, newly diagnosed with pulmonary TB and started on TB treatment during 2014 were sampled using systematic random sampling. Their TB and HIV care information was extracted from TB registers and HIV care cards. TB treatment success was summarized as proportions, and compared between rural and urban using Pearson's χ^2 test. To accommodate unequal probability sampling and correlation of patients within a clinic and adjusting for factors measured at clinic level: probability weighted mixed effects models with clinics as clusters were used to examine factors associated with TB treatment success.

Results: A total of 354 (65% males) and 265 (58% males) HIV-positive TB patients were sampled in rural and urban clinics respectively. TB treatment success in

rural and urban was 54% (53% among males, 55% females, $P = 0.625$) and 70% (68% among males, 74% females, $P = 0.426$) respectively ($P < 0.001$), subject to further data cleaning. Details on discrepancy between rural and urban success rates shall be presented.

Conclusions: TB treatment success rates are comparable between males and females co-infected with TB and HIV in Uganda. However, the success rate in rural compared to urban clinics is still low, thus need more attention.

EP-118-27 The impact of drug abuse on treatment outcomes of HIV-TB cases reported to the Hong Kong TB-HIV Registry, 2008-2013

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Background: People who live with HIV and abuse drugs have an increased risk of developing TB compared with non-drug users. Data on the impact of drug addiction on treatment outcomes of HIV-associated TB, however, are limited. We aim to examine retrospectively the association of drug addiction with TB treatment outcomes.

Methods: People who abuse drugs were recruited from a cohort of HIV-associated TB patients reported to Hong Kong TB HIV-Registry from 2008 to 2013. Three controls per case matched for age, sex and ethnicity were selected by stratified random sampling from the cohort. TB and HIV data and TB treatment outcomes were collected by review of standard programme record forms and medical records and compared using appropriate statistical methods.

Results: Of 175 HIV-associated TB patients reported to the TB-HIV Registry from 2008 to 2013, 18 (10.3%) were drug users. Patients who abused drugs ($n = 18$) and controls ($n = 53$) had comparable baseline disease characteristics with respect to case category, median CD4 count, extent of pulmonary lesions, proportion with a positive sputum AFB smear, bacillary drug resistance as well as proportion with HAART initiated within 8 weeks from date of start of TB treatment. Non-drug users were more likely to achieve favourable TB treatment outcomes (cure and treatment completion) (66.0% vs. 33.3%, $P = 0.015$) at 24 month.

Conclusions: People who abuse drugs constitute only a small proportion of HIV-associated TB cases reported to Hong Kong TB-HIV Registry but have a statistically worse treatment outcome compared to non-drug users. Intensified case management of HIV-associated TB patients who abuse drugs is warranted.

EP-119-27 Predictors of tuberculosis recurrence in adult patients treated in Nyanza Region, Kenya

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Background: Tuberculosis (TB) recurrence poses a major challenge to attainment of post-2015 Millennium Development Goals (MDG) targets of TB elimination in resource-limited settings. Understanding factors associated with TB recurrence are critical in order to reduce the burden of TB in Kenya.

Methods: Patients receiving TB care in Ministry of Health TB clinics in Nyanza Region, Kenya between April 2014 and January 2015 were eligible to be enrolled into a cross sectional study. TB treatment, adherence, lifestyle and socio-demographic characteristics were obtained by interview using a structured questionnaire. HIV status, use of antiretroviral therapy (ART) and other medical data were abstracted from the medical records. Patients with first episode of TB were considered as incident cases while patients with a previous history of TB diagnosis and treatment were considered recurrent cases. Univariate logistic regression was used to evaluate associations between patient characteristics and recurrent TB.

Results: We enrolled 278 out of 536 eligible patients of whom 227 were incident TB cases and 51 had recurrent TB. Median age was 32 years (IQR 26-40); 54% were male. Median time to TB recurrence was 4.3 years (IQR 1.2-10.4). HIV prevalence was higher among recurrent vs. incident TB cases (80% vs. 63%, $P = 0.015$). Coverage of ART was higher among those with recurrent vs. incident TB (95% vs. 82%, $P = 0.005$) Recurrent TB was associated with older age (OR 1.05/per year, 95%CI 1.02-1.07), male sex (OR 2.19, 95%CI 1.15-4.18) and HIV diagnosis (OR 2.47, 95%CI 1.18-5.19) There was less household crowding among those with recurrent TB (OR: 0.85/per household member, 95%CI 0.72-0.99). Current employment, cigarette smoking, alcohol use, poor TB drug adherence, or exposure to a known TB case was not associated with TB recurrence.

Conclusions: High prevalence of HIV infection among recurrent TB patients despite high ART coverage observed in this setting underscores the need for continued TB screening and prevention in this risk group.

03. Childhood MDR-TB, epi, detection, isoniazid preventive therapy and training

EP-120-27 Epidemiology of paediatric tuberculosis in the UK, 2000-2014

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Background: Children with TB can be difficult to diagnose and are more likely to develop severe disease. This study aimed to describe the epidemiology of tuberculosis (TB) in children in the UK (UK) over the past 15 years.

Methods: TB cases notified to the Enhanced Tuberculosis Surveillance System (ETS) between 2000 and 2014 were included. TB cases were categorized as: children (< 15 years), younger children (< 5 years), older children (5 to < 15 years), and adults (≥ 15 years). Patient and disease characteristics were described.

Results: Of all TB cases notified during the study period, 6061 (5%) were children. Childhood TB incidence declined from 3.4 cases per 100 000 in 2000 to 2.4 per 100 000 in 2014. The majority (68%) of all children were UK born, however the rate of TB in non-UK born children was 11 times higher than the rate in UK born children. Overall, 63.8% of all children had pulmonary disease, which was high compared with adults (55.6%). Children with TB had similar proportions of severe disease compared with adults, with the exception of cases with CNS meningitis (young children: 4% vs. adults: 2%). The most common ethnic groups for UK born children were White (25%), Pakistani (24%) and Black-African (21%); the most frequent countries of birth for non-UK born children were Somalia (25%), Pakistan (10%) and India (8%). Culture confirmation was low (24%), but was higher in non-UK born children (32%). Sputum smear status was known for only 30% of all pulmonary cases; a third were smear-positive. Overall, 73% of all children did not have their TB diagnosis confirmed by any laboratory method.

Conclusions: The epidemiology of TB in children differs to that of adults. The majority of children with TB in the UK were born in the UK. Of those, high proportions were of Pakistani and Black-African ethnicity. Information on sputum smear results and culture confirmation was low, and further development is required to improve diagnostic tests for TB in children.

EP-121-27 Epidemiology of pediatric multidrug-resistant tuberculosis in the United States, 1993-2014

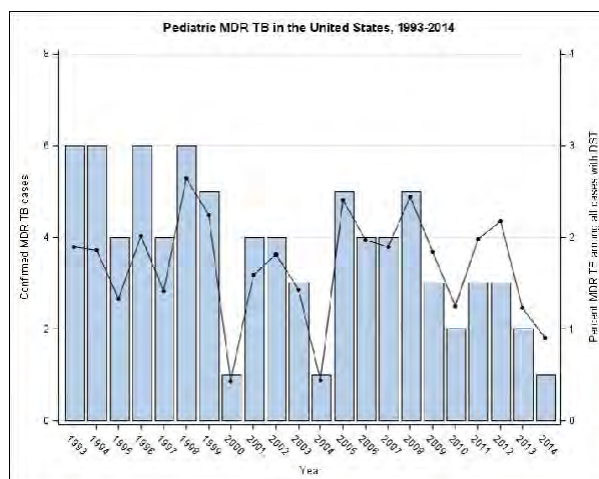
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Background: Multidrug-resistant tuberculosis (MDR-TB) is a public health threat worldwide. Accurate estimates of pediatric MDR-TB burden are unavailable due to challenges with microbiologic confirmation of disease. The aim of this analysis was to describe the epidemiology of pediatric MDR-TB in the United States since 1993.

Methods: We analyzed all newly diagnosed pediatric (< 15 years of age) TB cases reported to the US National TB Surveillance System (NTSS) from January 1, 1993, through December 31, 2014. Confirmed MDR-TB was defined as culture-confirmed TB disease caused by *Mycobacterium tuberculosis* resistant to isoniazid and rifampicin. End of treatment indicators from NTSS were used to estimate the percentages of confirmed MDR-TB cases who were alive at the time of diagnosis and initiated anti-TB treatment who had WHO-defined treatment outcomes.

Results: Of 20 789 pediatric cases in NTSS, 5162 (24.8%) had bacteriologically confirmed TB. Among 4862 (94.2%) with drug susceptibility test results, 82 (1.7%) had MDR-TB. Annually, there were 1 to 6 pediatric MDR-TB cases reported (0.4-2.6%) (Figure). Over 60% of pediatric MDR-TB was reported from five states. Most were female ($n=51$, 62.2%), one-third were Hispanic ($n=28$, 34.1%), and median age was 5 years (IQR 1-12). Over two thirds ($n=55$, 67.1%) were born in the US. Foreign-born cases ($n=27$) were born in 16 different countries. Most pediatric MDR-TB cases had additional resistance to ≥ 1 other first-line drug ($n=66$; 80.5%), one-third had resistance to ≥ 1 second-line drug (24/73 tested, 32.9%) and 3 of 54 tested (5.6%) had extensively drug-resistant TB. Of 76 with known treatment outcome, most cases successfully completed treatment ($n=64$ [84.2%]) and 12 (15.8%) had unfavorable treatment outcomes.

Conclusions: The number of pediatric MDR-TB cases in the US is declining. There was high treatment success despite the large proportion of cases with TB resistant to other first- and second-line drugs. However, only a quarter of pediatric TB cases had culture-confirmed TB disease, likely causing an underestimation of pediatric MDR-TB disease burden in the US.



EP-122-27 Evaluation of pediatric multidrug-resistant tuberculosis contact monitoring outcomes in Kyiv, Ukraine

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Background: Ukraine, a country of 43 million people, is among the top 5 countries in the world for burden of MDR-TB, with 25% primary MDR cases. Children less than five years old are at highest risk of developing disease after exposure to a close TB contact. Treatment for MDR-TB is lengthy and toxic with many side effects for developing children. Current policy in Ukraine is to monitor MDR-TB contacts for 2 years without treatment. New expert policy statements recommend treatment for high-risk contacts exposed to MDR-TB. We aimed to look at the outcomes of pediatric MDR-TB contacts registered within the Kyiv City Pediatric Tuberculosis Hospital from 2011-2015.

Design/methods: Data were collected on pediatric MDR-TB contacts registered at the Kyiv City Pediatric Tuberculosis Hospital during the five year period from January 2011 to December 2015. Patients diagnosed with active TB disease had data collected on demographics, type and duration of contact, BCG vaccination status, and comorbidities. We also recorded time to development of active TB symptoms, clinical manifestations of TB, source drug-susceptibility testing (DST), microbiological specimens and treatment regimen.

Results: Ninety-nine children were identified as MDR-TB contacts. Nineteen children aged 6 months to 16 years developed active MDR-TB, with a total of 12 of 19 aged < 5 years. A total of 11 of 19 were vaccinated with BCG and the majority presented with primary TB complex. Two of the 19 cases had microbiologically confirmed MDR-TB, the remainder were treated based

on contact DST. Three of 19 were exposed to cases of XDR-TB. The number of children referred as MDR-TB contacts increased from 6 in 2011 to 44 in 2015.

Conclusions: In this study, 19 cases of MDR-TB developed among 99 MDR-TB exposed children. Pediatric MDR-TB exposure is increasing yearly in Kyiv, Ukraine. Treating for TB infection before the development of disease is often thought of as an extravagant measure only performed in countries with a low burden of disease and high finances. With the high cost and morbidity of MDR-TB treatment, it is critical to reevaluate decisions to provide treatment to children exposed to MDR-TB.

EP-123-27 Effect of drug resistance on risk of *M. tuberculosis* transmission to young children

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Background: There are limited data on the risk of transmission comparing drug-susceptible (DS-TB) vs. multidrug-resistant *M. tuberculosis* (MDR-TB) strains. We compared the risk of infection and TB disease in children aged 0-5 years in household contact with an adult with bacteriologically confirmed MDR-TB vs. DS-TB.

Methods: In this cross-sectional analysis we included data from two community-based household contact investigation studies in Cape Town, South Africa. Children aged 0-5 years with documented household adult TB exposure enrolled between August 2008 and June 2011 were included. All adult index cases had bacteriological confirmation (sputum) and routine phenotypic/genotypic drug susceptibility testing. All children completed standard investigation for TB infection (Mantoux tuberculin skin test [TST]) and TB disease (symptom evaluation, chest radiography, bacteriology). TB disease was defined using standard case definitions. The impact of MDR-TB exposure and of each covariate on TST and TB disease status at baseline was assessed using univariable and multivariable logistic regression, with covariates in each model identified a priori.

Results: 473 children were included, 269 (56.9%) with DS-TB and 204 (43.1%) with MDR-TB exposure. Children with MDR-TB exposure were more likely to be TST positive (90/204; 44.1%) vs. 86/269 (32.0%, OR 1.52, 95%CI 1.07-2.16). Index case sputum smear positive status (AOR 2.23, 95%CI 1.33-3.73), child's age > 2 years (AOR 1.87, 95%CI 1.21-2.87), prior anti-tuberculosis treatment in the child (AOR 2.48, 95%CI

0.96-6.38) and MDR-TB exposure (AOR 1.84, 95%CI 1.16-2.92) were associated with increased odds of TB infection. A total of 12 (5.9%) of MDR-TB vs. 30 (11.2%) of DS-TB child contact had prevalent TB disease. In adjusted analysis HIV status (AOR 6.62, 95%CI 1.29-34.08) and index case smear positive status (AOR 2.75, 95%CI 1.12-6.72) were associated with increased odds of TB disease, while higher socioeconomic status (AOR 0.50, 95%CI 0.25-0.98) was protective. **Conclusions:** Our results suggest a higher risk of TB infection in child contacts with household MDR-TB vs. DS-TB exposure, not consistent with the notion of reduced 'virulence' in MDR-TB isolates. Diagnostic and treatment delay, and increased period of infectivity in household MDR-TB index cases, may explain the higher rates of TB infection in MDR-TB exposed children.

Risk factors	TST positive status		Prevalent TB disease	
	OR (95%)	Adjusted OR (95%)	OR (95%)	Adjusted OR (95%)
MDR-TB index case	1.52 (1.07-2.16)	1.84 (1.16-2.92)	0.52 (0.28-0.95)	0.42 (0.19-0.93)
Child's age	1.74 (1.20-2.53)	1.87 (1.21-2.87)	0.63 (0.36-1.10)	0.53 (0.27-1.03)
Prior antituberculosis treatment (child)	3.50 (1.60-7.70)	2.48 (0.96-6.38)	0.65 (0.15-2.83)	1.30 (0.26-6.40)
Index case smear positive	2.19 (1.41-3.42)	2.23 (1.33-3.73)	1.97 (0.90-4.31)	2.75 (1.12-6.72)
Child HIV positive	1.07 (0.25-4.52)	0.70 (0.15-3.33)	4.97 (1.20-20.51)	6.62 (1.29-34.08)
Child black African (vs. mixed race)	0.66 (0.44-0.99)	0.47 (0.27-0.83)	0.61 (0.31-1.22)	0.54 (0.20-1.45)
Socioeconomic status score (>5/11)	0.78 (0.55-1.11)	0.78 (0.52-1.16)	0.64 (0.36-1.12)	0.50 (0.25-0.98)

EP-124-27 Measuring the yield of an innovative TB REACH contact tracing strategy in Swaziland

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Background: Intensified case finding (ICF) is key to TB/HIV control. Few studies examine the association between index case (IC) age and number of contacts needed to screen (NNS) to detect or initiate anti-TB treatment (ATT) in tuberculosis (TB) cases in high-burden settings. With TB REACH funding, Baylor College of Medicine Children's Foundation-Swaziland (BCMCF-SD) evaluated methods to increase TB case detection and ATT initiation.

Methods: BCMCF-SD assessed the yield of household contact tracing of ICs receiving ATT in 7 TB clinics. Screening officers screened contacts for TB symptoms and referred symptom-positive contacts for further care. NNS was defined as the number of contacts screened to detect one additional TB case. Number needed to treat (NNT) was defined as the number of contacts screened to achieve ATT initiation in an additional TB case.

Results: 3255 ICs were linked to 12 175 contacts within 858 visited households. There were on average 4 contacts (median age 17.7 years; IQR 23.5-41.7) per IC. 40.2%

(4889/12 175) of contacts reported > 1 symptom consistent with TB. 56% (109/196) of additional TB cases were bacteriologically confirmed. Sub-group analysis demonstrated a 1.43 fold likelihood of detecting an additional TB case in HIV-affected households. NNS and NNT decreased as age of ICs and contacts increased (Table). 168 adult contacts were screened to detect 1 confirmed adult TB case, whereas 2040 pediatric contacts were screened to detect 1 adult TB case. More pediatric contacts (4080) than adult contacts (471) needed to be screened to achieve initiation of ATT by 1 contact aged 5-14 years.

Conclusion: The NNS, when calculated for adults, is consistent with WHO estimates. The increase in NNS as age decreased may reflect the low specificity of clinically diagnosed childhood TB or decreased pediatric transmission rates. In our setting, adult IC contact tracing provides greater yield than pediatric IC contact tracing.

Table Number needed to screen to detect one TB case

Index case age	Contact age		
	<5	5-15	≥ 15
<5	N/A	N/A	2040.17
5-15	N/A	3060.25	2448.20
>15	3060.25	720.06	167.68

EP-125-27 Implementation, challenges, and outcomes of a Stop TB Partnership TB REACH school-based TB contact tracing project in Swaziland

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Background and challenges to implementation: Swaziland's high incidence of tuberculosis (TB) and low case detection rate demonstrate the need for increased case finding. Despite national policy recommending contact tracing (CT) for TB index cases (IC), CT remains sub-optimal and no published evidence exists regarding school-based contact tracing (SBCT) in Swaziland. Perceived CT barriers include reporting bias, client stigma, and limited recognition regarding the importance of CT. In the second year of a TB REACH project, Baylor College of Medicine Children's Foundation-Swaziland (BCMCF-SD) partnered with the national School Health Programme (SHP) to perform SBCT at six schools in Swaziland.

Intervention: BCMCF-SD's CT program identified student IC attending a primary or secondary school. Schools were selected based on the IC's GeneXpert® (GXP) confirmation (prioritizing detected rifampicin resistance), age, and TB treatment duration. Each SBCT visit began with a school-wide TB educational session. Students then participated in TB symptom screening performed by a nurse or screening officer; those with a positive TB screen were requested to produce sputum.

Students also engaged in a soccer-based activity adapted from Kick TB/HIV's program. All sputum samples were analyzed using GXP technology.

Results and lessons learnt: Of the 2018 students symptom-screened for TB, 13.5% (272/2018) were identified with presumptive TB. Of these, 83% (226/272) produced sputum. GXP did not detect *Mycobacterium tuberculosis* in any sputum sample. Likely reflecting the natural school absence of severely ill children, no contacts were clinically diagnosed with TB. Challenges implementing SBCT included: scheduling restrictions due to exams, limited reliability of children's self-reporting of TB symptoms, demand from the schools to test all students without focusing on close contacts of IC, and reluctance of school staff to be screened for TB.

Conclusions and key recommendations: While CT remains a key component of effective TB control, populations with the highest additional yield should be targeted. In our setting, no additional cases were found via SBCT. Despite the lack of additional yield, this program effectively partnered with SHP and utilized educational activities to increase community awareness to TB risk factors and symptoms. BCMCF-SD's experience emphasizes the need to prioritize innovative, effective community-based CT methods.

EP-126-27 Empowering lay volunteers to implement a simple evaluation protocol to improve TB detection among hospitalized malnourished children in Malawi

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Background: Malnutrition is a major cause of morbidity and mortality in children. Mortality rates up to 30% have been recorded in Nutritional Rehabilitation Units (NRUs) in Malawi. Although tuberculosis (TB) is a major cause of childhood malnutrition, clinician shortages result in infrequent and incomplete evaluation among NRU patients. Teaching lay volunteers to recognize presumptive TB in malnourished children and prioritize them for evaluation using a simple protocol can increase TB case detection in understaffed, high-burden settings.

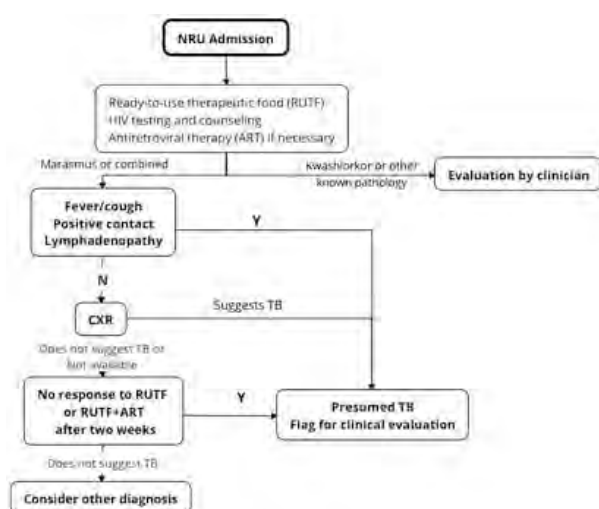
Intervention: We developed a basic protocol designed to guide lay volunteers to flag NRU patients with presumptive TB for clinical evaluation (Figure). Patients with marasmus or combined-type malnutrition were evaluated for the following: fever/cough; positive TB contact; or unexplained lymphadenopathy. The presence of any of these flagged that patient for clinical evaluation. In the absence of all three, a chest radiograph was done. If the chest radiograph findings suggested TB, or if the child did not respond to ready-to-use-therapeutic-feeds after two weeks of therapy, they were flagged as a presumptive TB

patient. Patients with kwashiorkor or known other pathology were evaluated by a clinician independent of this protocol.

Results and Lessons learned: A standardized TB detection protocol can effectively guide lay volunteers to streamline the diagnostic process in an NRU setting, reducing clinician involvement to interpretation and prescription of TB treatment. In the month prior to implementation, 8% (5/60) of NRU admissions were identified as presumptive TB. After protocol implementation, from October 2015-February 2016, 18% of total NRU admissions screened were identified as presumptive TB (60/335).

Conclusions: Use of lay volunteers was associated with an increased yield of TB case finding in children with marasmus malnutrition in the absence of a clinician in a high-volume, high-burden setting. This intervention has promise to shorten length of NRU stay, decrease treatment failure and improve TB and nutritional outcomes.

Figure Overview of NRU TB Screening Protocol



EP-127-27 Improving childhood TB detection, treatment and reporting using new tools, intensified screening and incentives

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Background: Detection of childhood TB has been a persistent challenge in Afghanistan due to the lack of appropriate diagnostics and insufficient number of trained healthcare workers. The TB REACH initiative funded a project to target child attendants at 15 public/private hospitals and 30 private practitioners in Kabul

and to introduce of advanced diagnostics (Digital X-ray and FM microscopes) and comprehensive diagnostic algorithm.

Intervention: The new equipment and reagents were procured and 181 doctors/nurses from both public and private hospitals were trained on childhood TB detection. Private pediatricians were approached to encourage referrals of children with presumptive TB. Transportation expenses of children referred from the private sector were reimbursed by the intervention. A small monetary incentive was made available to public-sector staff to encourage childhood TB detection and algorithm adherence. A pre/post analysis of official NTP notification data was conducted to measure the impact project activities had on childhood TB diagnosis, treatment and reporting.

Results: From 2013-2015, 803 669 children were screened for TB at hospital out-patient departments and private practitioner clinics, resulting in the identification of 17 028 (2%) children with presumptive TB who were then examined using X-ray and clinical evaluation. This detection rate is 3.5 fold higher than the years prior to the project. 2632 (15% of children with presumptive TB examined) were diagnosed with TB. Childhood TB notifications increased +288% (from 302 in pre-project to 1171) during the first year of activities and +384% (from 302 to 1461) during the second year. Though the project worked in a limited area, its impact can be seen nationally. Childhood TB notification rose from 3043 in 2012 to 4454 in 2014, a change of +46%.

Conclusion: Children with TB do access health facilities, but are mostly missed due to lack of advanced diagnostics and insufficiently trained and motivated health staff. These activities should be scaled up to other provinces in Afghanistan so children with TB are not missed by health services.

EP-128-27 Decentralization of HIV care through Option B+: operationalizing an opportunity to improve IPT uptake in children

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Background and challenges to implementation: Pediatric pulmonary tuberculosis (TB) remains a significant cause of morbidity and mortality globally. WHO recommends isoniazid preventive therapy (IPT) for the prevention of TB among children and adults. However, initiation and completion of IPT in children remains suboptimal, especially in countries with high rates of TB-HIV co-infection. Prevention of mother-to-child transmission of HIV (PMTCT) programs, particularly Option B+ programs that decentralize HIV care for women and

children, present an ideal opportunity for improving TB screening and IPT for children.

Intervention or response: To assess how TB screening and IPT are currently integrated into Option B+ programming, we conducted a desk review of HIV guidelines and Option B+ training curricula for 11 Sub-Saharan countries with the highest burden of TB/HIV co-infection.

Results and lessons learnt: HIV/PMTCT guidelines and curricula for all 11 countries were obtained. IPT: All countries have an IPT policy in place in either their TB or HIV guidelines, however, only four countries mentioned provision of IPT to children in their Option B+ training materials.

Pediatric TB Screening: All Option B+ training curricula mentioned screening pregnant women for TB in ANC settings, but only six countries additionally mentioned screening newborns or other TB-exposed children in ante- or post-pregnancy visits.

Symptom Screen: Adapting the standard WHO four symptom screen for TB to the pediatric population is essential in order to better identify children infected with TB. Only six countries adapted their TB screening questions as recommended by the latest pediatric TB guidance from WHO.

Conclusions and key recommendations: Screening children for TB, and ensuring that eligible children are appropriately initiated on IPT, continues to be a challenge for many countries. Option B+ offers regular and systematic opportunities to identify children who are at risk for TB and should receive IPT.

Figure 1. Implementation of Appropriate Pediatric TB Screening and IPT through Option B+ Programs

Country	HIV/TB Co-infection Rates ^a	Year of Option B+ Implementation ⁷	Inclusion of Pediatric TB screening and IPT in Option B+?	Recommend TB Symptom Screen Appropriate for Pediatric Population?
Botswana	60%	2015	Not mentioned	Not Mentioned
Lesotho	72%	2013	Not mentioned	Yes
Malawi	54%	2011	Not mentioned	Yes
Mozambique	52%	2013	TB Screen Yes; IPT Not Mentioned	Yes
Namibia	44%	2014	Not mentioned	Not Mentioned
South Africa	61%	2014	TB Screen Yes*; IPT Yes*	Yes
Swaziland	73%	2014	Not Mentioned	Yes
Tanzania	35%	2013	TB Screen Yes; IPT Not Mentioned	Not Mentioned
Uganda	45%	2013	TB Screen Yes; IPT Yes	Not Mentioned
Zambia	61%	2013	TB Screen Yes; IPT Yes	Yes
Zimbabwe	68%	2013	TB Screen Yes*; IPT Yes*	Not mentioned

*Specifically addresses infants born to mothers with TB, not inclusive of older children

NB: Disclaimer: The authors' views expressed in this publication do not necessarily reflect the views of the U.S. Agency for International Development (USAID) or the United States Government.

EP-129-27 TB Kids e-Training: operational implementation of The Union's online childhood TB course for health care workers in South Africa

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Background: The International Union Against Tuberculosis and Lung Disease (The Union) launched a free interactive computer-based childhood TB training course in March 2015, aimed at health care workers (HCWs) in primary/secondary levels of care. The biggest need for childhood TB training is in high-burden, low resource settings, where information technology (IT) experience and support may not always be readily available. We evaluated the feasibility of implementing a computer-based training course, and its impact on knowledge amongst HCWs in a high-burden TB district in the Eastern Cape Province, South Africa

Methods: Two-day training sessions were convened at a central computer laboratory (March-August 2015). Participants completed the course independently at their own pace. Knowledge evaluation was completed pre- and post-training with 60 multiple-choice questions.

Results: A total of 221 HCWs from all primary care service areas were enrolled and 220 (99.5%) completed both pre-and post-test evaluations. The mean age was 42 years (SD 11.8); 200 (91%) were female, 60 (27%) currently worked in TB services; only 48 (22%) had a personal email account. The mean baseline knowledge was 65% (SD 8%); the mean knowledge increase after training was 8% (95%CI 7.0-8.8, $P < 0.001$). Nurses below 40 years of age and those not working in TB services gained more knowledge than other nurses (3.1%; 95%CI 1.3-5.0, $P < 0.001$ and 3.7%; 95%CI 1.8-5.7, $P < 0.001$ respectively). Having a personal email account (proxy for IT exposure) did not have a significant impact on learning. Limited and unstable Internet capacity did not affect training; all participants were able to complete a downloadable desktop version of the course offline.

Conclusions: Given that basic IT requirements can be met, this course proved to be a versatile option that improved HCW knowledge of childhood TB. However trainee age may be an important factor contributing to technology use and effective learning that should be considered. IT access may be an obstacle in some settings. Attention should be given to evaluate setting-specific resources and requirements before rollout of computer-based training. Evaluation of knowledge translation into clinical practice is required. The impact of course facilitation for contextualization and consolidation of

knowledge gained through training is important to consider in the future.

04. Revolution: harnessing mobile technologies to support client-centred care

EP-130-27 The use of mobile applications in patient-centred care: experience from a pilot in Beijing, China

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Background: Conventional TB patient management approaches based on Directly Observed Treatment (DOT) are not always feasible in all settings and not really patient-friendly. On the other hand, mobile internet technique, through its extensive use, convenient networking, instant messaging, accurate delivery, less geographical restrictions and strong privacy, offers an innovative option for TB programs to provide more effective, more patient friendly services.

Methods: The Clinical Center on Tuberculosis, China CDC (CCTB) developed a mobile terminal application (APP) which has 4 functions: 1) remind drug taking and follow-up visit; 2) promote communication between doctors and patients; 3) provide health knowledge, and 4) generate electronic medication card to make doctors know how the treatment compliance is. CCTB conducted a pilot on using patient management APP in Beijing Tongzhou district and Beijing Chest Hospital from December 2015 to March 2016. Eligible newly registered TB cases are educated and encouraged to install the APP, and management responsibilities are assigned to relevant community health workers. Patients' drug taking information is collected and analyzed through the use of APP in patients and community health workers.

Results: In Beijing Chest Hospital, 148 new TB cases were registered and 112 of them have installed APP (44 patients installed IOS terminals and 68 installed Android terminals). 10 patients did not install APP because they do not have smart phones and 16 patients rejected to install due to different reasons. 84 patients submitted the drug taking information, and average drug taking rate is 75%. In Tongzhou district, among 51 new cases, 42 installed APP and 8 do not have smart phones. One patient refused to install the APP. 19 patients submitted the feedback on drug taking and the average drug taking rate is 45%. By using the APP, the connection capacity between hospital and TB dispensary on patients management is improved, which results in reduction of workload for medical staffs, the decrease of default for TB patients and the reduction of transmission risk.

Conclusions: The popularization of smart phone provides great potential for innovative patient centered care. Future efforts will focus on effectiveness analysis, and the

data connection between APP, TB dispensary and hospital information system.

EP-131-27 Utilizing a full complement of communication strategies to maintain mobile patients in care

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Background and challenges to implementation: Patient mobility can lead to a rupture in continuity of treatment resulting in an increased risk of transmission and worsening of disease. Health Network (HN) was developed to maintain mobile patients in TB care even as they migrate for employment, family reunification or pursuit of safe haven. Since, its inception over 20 years ago, HN has experimented with a variety of communication technologies in order to maintain continuity of care. While health care systems have touted cutting edge technologies, globally access to the most fundamental methods of communication can be tenuous. In more recent years, with advances in internet communication and the ubiquitous nature of mobile phones, patient case management is easier to initiate and maintain.

Intervention or response: HN utilizes case managers located in Austin, TX, to provide continuity of care to more than 800 patients per year under treatment for TB disease or infection. Regular communication occurs between HN, patients and providers utilizing fax, encrypted email, landlines, cell phones, texting, Skype, Viber, Google Chat, Facebook messaging and others. Through consistent evaluation, the program has learned it must utilize a variety of technologies in order to communicate with individuals and sites with multiple needs and access to resources.

Results and lessons learnt: Documented rates of treatment completion for TB disease over the previous 10 years have remained strong with an average of 84% rate of completion. This has been accomplished through the consistent application of HN protocols and the flexibility to incorporate new communication strategies identified by a patient, provider or outside experts.

Conclusions and key recommendations: An effective mobile case management system is most successful when it employs communication technologies spanning from very low tech to highly sophisticated. The key is allowing patients and providers to identify the most effective communication platform greatly advances the possibility of treatment completion. Supporting the patient as an active member of the case management team by following her lead in the selection of communication method that best suits her day-to-day reality.

EP-132-27 Electronic monitoring of medication adherence for tuberculosis treatment in Morocco: a pilot study

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Background: Non-adherence to treatment of tuberculosis (TB) is a major barrier to TB control.

Objective: We investigated the effectiveness of the Medication Event Monitoring System (MEMS) as a tailored adherence-promoting intervention for improving patients' adherence to TB treatment in Morocco.

Method: The outcome of TB treatment were compared between the patients who received MEMS and the patients who received standard TB care among patients confirmed by sputum acid fast bacilli smear. Standard TB care was based on directly observed treatment (DOT) and self-administration-treatment. Results of participants, recruited between April 2014 and August 2015, were retrospectively analyzed. The patients from 5 health centers who received MEMS (MEMS group) were compared with the patients from 7 health centers who received standard of care (control group) during same period in Morocco, Sale region.

Results: One hundred and three patients in MEMS group and 161 patients in control group were compared. The mean age (37.2 ± 16.3 vs. 36.1 ± 15.9) and the male-to-female ratio (73:30 vs. 111:50) were not different between the two groups. The mean adherence rate in MEMS group was 94.3%. The cure rate and the completion rate in MEMS group were 33.7%, and 64.4%, respectively. Those in control group were 12.4%, and 65.2%, respectively. The default rate were significantly lower in MEMS group than in control group: 1% (1/103) vs. 19.3% (31/161), OR = 0.04 (0.01-0.31), $P < 0.01$.

Conclusion: MEMS could reduce the default rate of infectious TB patients in Morocco, Sale region.

EP-133-27 Using mobile phones to ensure that referred tuberculosis patients reach their treatment facilities: a call that makes a difference

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Background: Over the last decade, the availability and use of mobile phones have grown exponentially and in Cambodia, there are now 20 million mobile phone subscriptions in a population of 14 million. In the Sihanouk Hospital Centre of Hope (SHCH) in Cambodia about half of all tuberculosis (TB) patients referred out to peripheral health facilities for TB treatment initiation or continuation are lost to contact after referral (LTCR) [‘missed cases’]. We hypothesized that use of mobile phone tracking could reduce such missed cases. We thus determined the number and proportion of 1) referred TB patients who could be contacted through a mobile phone and 2) LTCR among referred patients (for TB treatment initiation and continuation) before and after the introduction of mobile phone tracking.

Methods: A before-and-after follow-up study involving TB patients referred out from SHCH to peripheral health facilities during January-December 2013 (the before period) and May-October 2014 (the intervention period). Standard operating procedures were used to contact individual patients and/or health facilities using a mobile phone.

Results: In 2014, among 109 TB patients referred to peripheral health facilities, 107 (98%) had access to a mobile phone, of whom 103 (97%) could be contacted directly while five (2%) were contacted through their health care providers. A total of 108 (99%) of 109 referred TB patients in the intervention period were thus reportedly placed on TB treatment compared to 106 (37%) of 290 referred TB patients in the pre-intervention period ($P < 0.001$). Tracking approximately two referred TB patients using mobile phones prevented one missed case.

Conclusions: Using mobile phones to ensure that referred TB patients reach their treatment facilities proved worthwhile. This is a useful way forward for improving retention of TB patients in the programme.

EP-134-27 Mobile text messaging for joint interventions on tuberculosis and tobacco control

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Background & Challenges: Tobacco smoking is an established risk for tuberculosis (TB) reactivation and for death in TB patients. Individuals who stop smoking can reduce these risks. Joint action on TB and tobacco control can thus be beneficial for the prevention of both diseases. However, integrating such initiatives into the routine work of national TB programmes and health promotion units responsible for smoking cessation programmes involves challenges due to cost and human capacity. Achieving the ambitious targets of the End TB Strategy will require innovative approaches to render current approaches more effective. Digital technology

presents new opportunities for different aspects of TB prevention and care, including smoking cessation. The rapid, unprecedented growth of mobile phone ownership and usage across low and middle-income countries brings such interventions within the reach of many programmes. Text messaging could have a role in informing patients and health professionals, and promoting healthy behaviours, such as smoking cessation across a broad cross-section of target groups.

Intervention or response: The presentation discusses how a text message library for mobile phones is being built through multi-partner collaboration, targeting both the national TB and tobacco cessation programmes. The approach for developing the prototype text messages was based on a simulation exercise, using a patient-centred model with different entry points in a typical pathway that an individual seeking care would follow. The presentation will further discuss how the text-based message interventions will be implemented in 2 countries and data will be collected to evaluate input and feed it back to improve the intervention.

Results and lessons learnt: We discuss the opportunities and challenges in developing a validated message library that is intended to be integrated into existing mobile health solutions in countries. The messages are also designed to target tobacco users and support them to stop smoking through existing TB programmes.

Conclusions and key recommendations: In addition to promoting digital health as a vehicle for joint efforts towards the prevention and management of TB and tobacco consumption, the presentation will discuss implementation issues which would be critical so that the experience in the pathfinder countries can be reproduced elsewhere.

EP-135-27 Treatment adherence among TB patients in the private sector: a combination of technology and human touch

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Background and challenges to implementation: Under the aegis of Municipal Corporation of Greater Mumbai (MCGM), the Private Provider Interface Agency model (PPIA) has been active since September 2014. PPIA staff engage with private health care providers to support early diagnosis, prompt treatment and timely notification of TB patients to government of India. Prior to this intervention, there was limited or no private provider initiated follow-up of TB patients. The PPIA services include several strategies for adherence support to facilitate treatment completion.

Intervention or response: The PPIA provides multi-layered patient-centric adherence intervention support to privately-treated TB patients. First line anti-TB drugs prescribed by private providers based on Standards of TB Care in India (STCI) are made available to patients free of cost via e-vouchers that are paid for by the PPIA.

Notification via call center prompt a menu of support services including refill-tracking, initial home visit, patient and family counseling, reminder text messages to patient mobile phones, automated tracking of drug refills, weekly calls by contact center to patients for self-reported adherence, and as-required home visits. This menu of adherence support services ensure focus on treatment adherence and retrieval of treatment interrupters. Since drugs are given to patients on a monthly basis, refill completion is also tracked. Patient wise adherence scores, dashboards and reports help in monitoring patient treatment adherence.

Results and lessons learnt: From December 2014 to May 2015, 71% (913/1282) new bacteriologically confirmed TB patients successfully completed at least 6-months anti-tuberculosis treatment, and 167 (13%) were transitioned to public care for standard witnessed dosing. 14% (177 patients) were lost to follow-up. There were favorable treatment outcomes for 86% of patients.

Conclusions and key recommendations: Patient-centered multi-layered adherence support is feasible even among privately-treated TB patients in India, with a combination of technology and human touch. Integration of pill-in-hand adherence monitoring systems planned for this year will further improve data timeliness and quality.

Figure Treatment adherence: 3-pronged approach



EP-136-27 Factors contributing to good TB treatment adherence among patients in North West Region of Cameroon

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Background: Until 1988, the control of Tuberculosis (TB) in Cameroon was borne exclusively by the Ministry of Public Health (MoPH). This comprised diagnosis and treatment as well as cost free health facility related admissions. The economic and financial crises in the late 1980s led to a sharp drop in core funding by the MoPH. The setting of this study was in North West Region (NWR) of Cameroon with a population of about 2 038 733. It is one of the 11 TB epidemiological regions of

Cameroon and comprises 21 of the 230 Diagnostic and Treatment Centers (DTCs) that are in Cameroon. TB causes tremendous suffering worldwide, especially in low- and middle-income countries.

Methods: A convenient sample of 38 adult TB patients and 18 TB treatment nurses were recruited in the study. In-depth semi-structured interviews were conducted for all study participants. In addition, four focus group discussions (FGDs) were held for three groups of 10 patients each and one group of 10 TB nurses.

Results: From this qualitative assessment, several factors were identified that may potentially contribute to the relatively high TB treatment adherence in this region. From the in-depth interviews administered to TB patients, a majority of patients reported taking their medicine on their own, without a designated treatment supporter, by using an alarm system to remind them of the time to take their treatment (21/38 respondents). In addition, the TB nurses surveyed indicated a high level of knowledge about the correct administration of TB treatment including the importance of TB treatment adherence. The patients surveyed also had good knowledge of most aspects of tuberculosis treatment reported little or no feeling of stigmatization by their families or communities due to the disease and reported a good patient-health service staff relationship during the FGDs.

Conclusions: These results suggest that in similar settings where TB treatment administration is not directly supervised by a healthcare worker, high rates of treatment adherence and completion may be achieved by other methods, including patient use of mobile phone alarms as treatment reminders and strong engagement by health care workers in patient education at treatment initiation.

EP-137-27 Mobile banking system to aid MDR-TB patients and DOT providers can help TB program to save time and money

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Background and challenges to implementation: Minimum incentive to the DR-TB supporter/ DR-TB DOT provider and nutritional support to DR-TB has been shown to be effective to bring good results. As per Bangladesh NTP policy, DR-TB DOT providers receive a monthly allowance and the patients also receive an allowance to buy supplemental food for nutrition. But it is troublesome or sometimes impossible to distribute this money manually, especially where the numbers of patients are large and communication (transport) system is poor, as in Bangladesh.

Intervention or response: Considering the needs of the program, on behalf of the NTP Bangladesh TB CARE II project has made an MOU with a renowned bank that operates a network of ATMs and mobile cash transfer systems all over the country, even in the remotest areas of Bangladesh. During the starting of treatment, all the personal data of the MDR-TB patients and DOT providers have been collected and with the help of Bank

staff, mobile money accounts have been opened for all. The transition to mobile cash transfer came into effect in November 2013 and is continuing smoothly to date.

Results and lessons learnt: Currently, 688 DOT providers and 744 patients across 34 districts and 5 city corporations receive their allowances regularly and on time through the mobile cash. Carrying cash around was a big risk and it took a good amount of time to go to different providers and patients. The disbursements of funds that used to take more than a month is now a matter of only two days through the mobile money transfer system. The beneficiaries can count on a regular allowance and the program staff can devote time once spent distributing cash to other program activities.

Conclusions and key recommendations: The system is quick, reliable and verifiable. The mobile banking system can make life easier—not only for the program but also for the patients and DOT providers, who can now access their funds with a quick visit to an ATM or mobile banking agent.

EP-138-27 SMS for sure: Use of mHealth for tuberculosis care in Delhi, India

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Background: Mobile health (mHealth) represents an innovative tool in the fight against tuberculosis (TB), and it is in countries where TB prevalence is highest that mHealth initiatives stand to make the greatest impact. The Revised National Tuberculosis Control Program Delhi rolled out mobile technology for providing quality TB care to its patients in November 2015. This study aims to evaluate the effect of mobile technology and Short Messaging Service (SMS) on improvement in TB treatment adherence among new TB patients enrolled under TB program in Delhi.

Intervention: In the observational study, all the new TB patients (Pulmonary and Extra Pulmonary TB) were enrolled for the period November 2015 to February 2016 after informed consent. The study was supported with a server set up, toll free number generation and counselors for provider and patient feedback. Patients were randomized in three groups using the SAS program. Group 1: received enrollment confirmation SMS, weekly motivational SMS, reminder SMS for missed dose. Group 2: received enrollment confirmation SMS, reminder SMS for missed dose. Group 3: received no SMS. Each patient record was analyzed using a unique ID generated in Optimax system. The endpoint defined for the study was the medication adherence rate assessed based on number of missed doses reported by the server among the enrolled patients. Statistical analysis was performed using one sided Fischer's Exact Test.

Result: In the study period, 6000 new TB patients were registered in the program. Out of them, 3118 (34%) patients gave consent for enrollment in the study. They were randomized into the three groups. Medication

adherence rate was highest in Group 1 and Group 2, who were supported with SMS for TB care. Overall missed doses among all the three groups were only 42 (1.34%) as compared to the State program average of 5% among the registered new TB patients in the same time period previous year.

Conclusion: mHealth affects appropriate TB care and management as is evident by the significant reduction in missed doses and improved adherence to TB treatment. The technology needs to be replicated for all TB patients in high work load settings.

EP-139-27 Utilization of information on tuberculosis disease, available diagnostic and treatment services among helpline callers in five states of India

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Background: In March 2014, Project Axshya initiated a tuberculosis (TB) helpline to improve TB knowledge and community reach to TB diagnostic and treatment services. Health systems are of a complex nature and introduction of technological solutions needs to be appropriate for those seeking such services. Hence a research study was conducted in five states of India to understand the utilization of TB related information by helpline callers.

Methods: A retrospective exploratory study was conducted in June 2015. 205 callers with completed call status from February to March 2015 database were sampled through random sampling method. Quantitative data on type of information sought by callers, utilization of this information, needs and suggestions on helpline services were collected through telephonic interview of 10 minutes. Analysis was done through descriptive statistics in SPSS software.

Results: Of the total ($n = 205$), 98% of helpline callers were literate; the average age of helpline callers was 32 years, and 94% of callers were male. Of the total ($n = 205$) 91% callers called helpline to obtain knowledge on tuberculosis, 81% callers sought information on signs and symptoms of TB disease and 30% on available diagnostic and treatment services. A positive relationship ($r = +0.558$) has been found between information sought on TB disease and the utilization of health services by callers; 60% of callers had referred others to TB diagnostic centers, while 58% accessed TB diagnostic and treatment center for themselves. Of the total ($n = 205$), 54% of callers needed updated information on the prevention, symptoms, diagnosis, treatment, course of TB disease and 43% gave suggestions on the improvement of quality of helpline service through trained helpline executives.

Conclusions: Helpline offers privacy, protecting the callers' identity and empowers them to take their own health decision. Intervention is effective in motivating

people to visit health center for TB testing. Advocacy strategies on helpline intervention should focus on reaching non-callers like females, illiterates and people in vulnerable age group.

05. Better TB services for better treatment outcomes

EP-141-27 Narrowing the gap between cure and treatment success over four years: sign of improved quality of TB treatment follow-up

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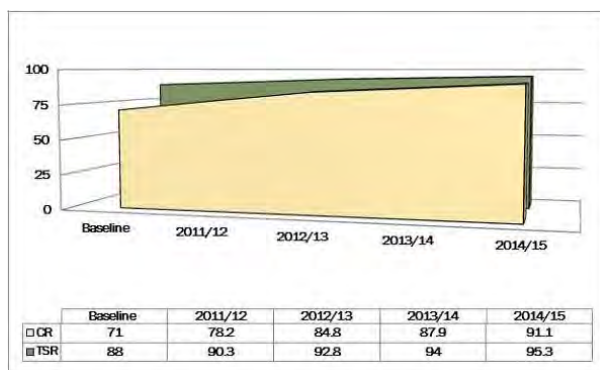
Background: The USAID-funded Help Ethiopia Address the Low Performance of TB (HEAL TB) project in collaboration with the national TB program has been supporting comprehensive TB prevention and control interventions in two regions of Ethiopia, covering 50% of Ethiopia's population of 90 million since 2011. We present the trends in cure and treatment success rates for drug sensitive TB in the 10 zones that were included in the initial phase of project implementation in 2011/2012.

Interventions: HEAL TB's support included capacity building for TB program managers at different levels, training of health professionals, expansion of diagnostic laboratory centers including quality assurance, and mentoring and supportive supervision. The project also provided recording and reporting forms for health facilities.

Results and lessons learnt: HEAL TB supported treatment of 39 283 new smear positive (SS+) pulmonary TB patients in 10 zones during October 2011 to September 2015. Treatment success rate (TSR) for SS+ improved from 88% at baseline to 95.3% at the end of the fourth project year, and the corresponding cure rate (CR) increased from 71% to 91.1%. The increase in CR over four years was 28.3%, which is significantly higher than the 8.3% increase in TSR ($P < 0.001$). The gap between treatment success and cure narrowed significantly over the four years: a difference between TSR and cure rate of 17% at baseline to 4.2% at the fourth year (Figure). The improvement in cure rate is attributed to the improved knowledge of health workers on patient follow up and the availability of quality assured laboratory services.

Conclusion: The comprehensive project support, including expansion of quality assured laboratory services, enabled the narrowing of the gap between cure and treatment success. It is a demonstration of the significantly improved quality of follow up of TB patients on treatment.

Figure Trend of cure rate and TSR among patients



EP-142-27 Gender differences in tuberculosis diagnosis and treatment in an industrialised low-incidence setting: Victoria, Australia, 2002-2014

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Background: Early diagnosis and treatment are essential for effective tuberculosis management. Gender disparities have been identified in tuberculosis research internationally indicating that women have delayed diagnosis following presentation to healthcare, compared to men. We sought to explore gender disparities, predominantly at the health care provider level, in Victoria, a low-incidence setting with universal healthcare.

Methods: Retrospective cohort study, 2002-2014. Gender was included as independent variable in statistical analyses in addition to demographic, clinical, pathological and risk factor characteristics. Survival analyses were used to assess various time periods from symptom onset, healthcare presentation, investigations and treatment commencement. Multivariate logistic regression was used to analyse symptoms, laboratory tests, treatment regimens and treatment outcomes.

Results: Multivariate analyses revealed several significant gender disparities. Males began treatment sooner after healthcare presentation than females (Hazard ratio [HR] 1.14 $P < 0.001$, 95%CI 1.06-1.23) and had a specimen collected sooner (HR 1.13 $P = 0.004$, 95%CI 1.04-1.22). Considering cases with pulmonary involvement: males were more likely to have a chest X-ray sooner (HR 1.14 $P = 0.038$, 95%CI 1.01-1.30); and a sputum sample collected sooner (HR 1.19, $P = 0.010$, 95%CI 1.04-1.36); but were less likely to have a positive sputum sample (OR 0.80 $P = 0.044$, 95%CI 0.65-0.99). Gender was not a significant predictor of cavitation (OR 1.07, $P = 0.566$, 95%CI 0.85-1.33); nor of having symptoms of cough (OR 1.06, $P = 0.842$, 95%CI 0.58-1.96) or sputum (OR 1.00, $P = 0.997$, 95%CI 0.65-

1.54); nor of the time between symptom onset and healthcare presentation (HR 1.12, $P = 0.152$, 95%CI 0.96-1.31) (symptom data only available 2012-2014). Males were more likely to die during TB treatment than females (OR 1.73 $P = 0.007$, 95%CI 1.16-2.57). The time from the first positive laboratory or CXR result until treatment commencement was not significantly different between genders (HR 0.99 $P = 0.798$, 95%CI 0.89-1.10).

Conclusions: Significant disparities were detected in the time to diagnosis of males vs. females, but no disparity was detected between diagnosis and treatment commencement. More research is needed to determine how the complex interplay of practitioner and patient health-related beliefs and behaviours contribute to these differences, and into developing strategies to reduce gender impact.

EP-143-27 Investigation of non-conversion for bacteriologically confirmed tuberculosis in Emfuleni Sub-District, Gauteng, South Africa

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Background: USAID TB CARE II provides technical supported to selected facilities in Sedibeng District, Gauteng, South Africa. The support consists of facility mentoring on TB and TB/HIV recording and reporting, and routine record audits and monitoring of programme progress through a district rapid assessment tool. A study was conducted to assess the management of patients with newly-diagnosed, bacteriologically-confirmed drug-sensitive tuberculosis (TB) whose sputum did not convert after two months' treatment. National TB management guidelines recommend examination of sputum from such patients should be investigated using line-probe assay (LPA) and culture and drug susceptibility testing.

Methods: Medical and laboratory records of new and re-treatment bacteriologically-confirmed TB patients registered between January and October 2015 were reviewed. The electronic TB register (ETR.net) was used to generate the list of patient remaining smear-positive after two months treatment. Adherence to national guidelines on the management of TB and TB/HIV was measured in terms of the types and frequency of investigations performed during the course of treatment, including LPA and culture investigations.

Results: All 66 patients who failed to achieve sputum smear conversion after two months treatment had an HIV test result, and of these, 33 (50%) were HIV positive; of HIV-positive TB patients, 32 (96.9%) received both antiretroviral therapy (ART) and cotrimoxazole preventive therapy (CPT). Only 28 (44.4%) of non-converters had their sputum examined using LPA and culture. Drug resistance was low, with only two cases of drug resistance, one of isoniazid monoresistance and another of rifampicin monoresistance.

Conclusions: There was sub-optimal adherence to national guidelines when monitoring newly-diagnosed bacteriologically confirmed TB patients who fail to convert after two months treatment. Ongoing mentoring and on-the-job training are needed to improve the quality of TB services provided in these facilities.

Table Sputum non-conversion at 2 months ($n = 66$)

Indicator	Number (%)
Bacillary load +++	37 (56.1)
Bacillary load <+++	26 (39.4)
Positive HIV result	33 (50)
LPA/sputum culture done	28 (46.7)

EP-144-27 TB treatment strategies and risk of default: a quasi-experimental study

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Background: Tuberculosis (TB) still represents a major problem in Latin America. From 1998 to 2014, success and default rates ranged from 53-74% and 15-20% respectively in high burden areas of Buenos Aires, which concentrates half of 10.000 cases per year in Argentina and implements direct observation of treatment (DOT) in only 30% of patients. Poor adherence represents a major threat for TB control and promotes emergence of drug resistant tuberculosis. DOT has been a fundamental component of the WHO Stop TB strategy; however its effectiveness to improve treatment outcomes and its successful implementation have generated debate and controversy.

Objective: To evaluate DOT or mixed strategies compared to self-administered (SAT)) and the implementation of a subsidy on the risk of treatment default in TB patients.

Methods: Follow up of patients with first treatment of pulmonary TB in 47 health care centers. We used multilevel logistic regression to control for specific individual and system level factors to estimate the adjusted effects in high and low risk subgroups.

Results: We included 962 patients (SAT 636, DOT 185 and Mixed 141). Default rates were 20% in the SAT, 8.5% in the DOT and 7% in the mixed group (adjusted OR 0.41 [95%CI 0.21-0.78] and 0.36 [95%CI 0.18-0.77]) and it was 11% in the subsidy group vs. 20.2% without (adjusted OR 0.39 [95%CI 0.25-0.60] . Other variables associated with higher default rates were drug and alcohol use, young age, hospital vs. primary care center, income and lack of insurance. The protective effect of DOT and mixed treatment was especially marked in high risk subgroup.

Conclusions: Both DOT and mixed treatment and a direct financial aid were associated with substantially lower odds of default. The high rate in the SAT group is cause for great concern, since this is the choice for the majority of patients. Successful TB control cannot be reduced to recommended treatment modalities. Identifying barriers to DOT implementation and evaluating risk factors at the individual and system levels may provide essential information to design feasible and context relevant interventions to improve control and reduce resistance.

EP-145-27 Isoniazid and ethionamide resistant mutations are associated with poor treatment outcomes among MDR-TB patients in South Africa

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Background: Ethionamide (ETH) is part of the backbone regimen used for treatment of multidrug-resistant TB (MDR-TB). Resistance to isoniazid (INH) among MDR-TB patients may cause ETH to be ineffective, as both are pro-drugs activated by *inhA* gene and mutations within this gene may lead to their cross-resistance. Furthermore ETH resistance is caused by mutations within *ethA* and *ethR* genes forming part of the ETH drug activation pathway. Phenotypic drug susceptibility testing (DST) of ETH is difficult and often unreliable. We used deep sequencing to compare *inhA*, *ethA* and *ethR* genetic regions in serial isolates (baseline and follow-up) with treatment outcomes.

Methods: Serial isolates from 46 MDR-TB patients initiating treatment containing ETH in the regimen were collected between 2005 and 2009. Unfavourable treatment outcomes was defined as death, default and failure, while favourable was cure and treatment completion. All isolates were phenotypically resistant to rifampicin and INH. Genotypic DST was extracted from data generated from deep sequencing by the Illumina method. The Barrons-Wheeler aligner was used to align the sequences to H37Rv reference strain and Pilon generated single nucleotide polymorphisms, insertions and deletions in *ethA*, *ethR* and *inhA* genetic regions. Cross-resistance was defined as the presence of both *inhA* and either *ethA*, *ethR* mutations in clinical isolates.

Results: Most patients, 29/46 (63.0%), had unfavourable outcomes, 13 (28.3%), had favourable outcomes, while 4 (8.7%) had unknown outcomes. Genotypic analysis revealed non-synonymous, insertions and deletions within *ethA*, *ethR* and *inhA* promoter regions. The mutations were detected in 27 (59.0%) and 23 (50.0%) of ETH and INH associated regions respectively. The majority of mutations causing ETH 20/29 (68.9%) and INH 18/29 (62.1%) resistance occurred among patients with unfavourable outcomes. Both *inhA* and either *ethA* or *ethR* mutations were detected in 16/29 (55.2%) of

patients with unfavourable outcome. Cross-resistance of both INH and ETH drugs was associated with unfavourable ($P = 0.021$) with 16/29 (55.2%) compared to 2/13 (15.4%) who had favourable treatment outcome.

Conclusions: Baseline ETH molecular resistance before treatment is a concern. The unfavourable treatment outcomes of patients with both *ethA*, *ethR* and *inhA* mutations highlights the importance of genotypic testing before initiation of treatment containing ETH regimens.

EP-146-27 Development and validation of a complexity scale to improve management of vulnerable TB patients in the North West of England

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Background: In England, TB disproportionately affects those with social risk factors for disease. The North West of England contains some of the most deprived neighbourhoods in the country and has high TB incidence in some urban centres. Early identification of TB cases with complex disease is critical to provide Enhanced Case Management, a package of supportive interventions to improve treatment outcomes. We set out to develop and evaluate a brief scale measure of complexity that could be used to prioritise delivery of Enhanced Case Management services.

Methods: As part of the North West TB Cohort Review, between April 2013 and July 2015, data on ten potential indicators of clinical and social complexity were systematically recorded from all notified TB cases in the region. We used χ^2 testing and principal components analysis to construct a scale measure of complexity, and logistic regression models to evaluate the performance of the scale in predicting TB treatment outcomes.

Results: In total, 1714 cases were notified, of whom 44.5% had at least one of the ten potential indicators of complexity. After removing one item that was statistically uninformative to the scale construct (language barrier), the final complexity scale comprised of nine items (medical comorbidities, previous TB diagnosis, mental health problems, non-adherence to medication, imprisonment, problem alcohol use, IV drug use, homelessness and hard to reach group [HTRG]) with good internal consistency (Cronbach's alpha 0.7). Higher complexity scores were significantly associated with lower odds of completing treatment within 12 months (OR 0.25, 95%CI 0.14-0.46) and higher odds of being lost to follow-up (OR 4.97, 95%CI 2.05-12.06).

Conclusions: Clinical and social complexity was common in TB cases in the North West of England. Our brief scale measure of complexity was able to distinguish those likely to have poor treatment outcomes over the following 12 months and could be used to rapidly

identify individuals likely to benefit from Enhanced Case Management because of clinically and/or socially complex care needs. We envisage the complexity scale being widely used to improve delivery of effective TB care, and to monitor progress in tackling social determinants of TB in England.

EP-147-27 Causes and determinants of loss to follow-up among tuberculosis patients in Khartoum State, 2013

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Background: The success of the DOT system continues to be hindered by the TB patient lost to follow-up rate in Khartoum State between 60% to 15% during the last five years. It was found that a total of 900 patients were defaulting from a total of 5911 patient in 2013. Despite the existing information about the causes of loss to follow-up and the endless efforts and solutions put to decrease its rate. Using the direct causes and the existing information obtained from the DOT system statistical records, this project looked into the loss to follow-up rate and understanding the determinants of its causes.

Methods: A descriptive longitudinal cross sectional study was conducted in 2013 in Khartoum state, it aimed to understand the causes and determinant of loss to follow-up among TB patients. TB patients who were lost to follow-up were interviewed by phone using a structural questionnaire. The data collectors took patients contact from the TB register.

Results: The reason why those TB patient lost follow-up was 47 (27.6%) were dead, Others were living outside Khartoum state 25 (14.7%) and they travelled back home, about 24 (14.1%) said they finished their treatment and there was an error in the records, 28 (16.4%) they said because of the treatment outcome, financial issues was one of the reasons in 10 patients (5.8%), and 11 (6.5%) said due to the lack of services near their households About 9 (5.3%) said they don't have anyone to go with them to the TBMs, some of them said the doctor who told them to stop the treatment 8 (4.7%), while 6 (3.5%) because of work, 2 (1.2%) said that they stopped because of fasting in Ramadan.

Conclusions: Addressing the determinants of lost to follow-up of TB patients in Khartoum state mainly due to lack of awareness in the disease knowledge and communication between the TB patients and health workers, which need to intervene such as supervision visits and increase the involvement of the health voluntaries. There is a need to develop electronic register and unique identification number for each TB patients which reduce the redundancy and enhance the tracing of patients.

EP-235-27 Determinants of loss to follow-up and pathways to care during an intensified case finding study in Dar es Salaam, Tanzania

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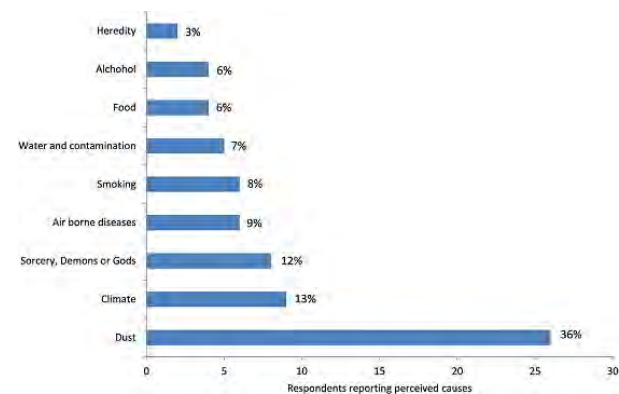
Background: Presumptive tuberculosis (TB) patients in low-income settings have complex pathways to health care that often result in diagnostic delay and continued TB transmission in the community. We studied determinants of loss to follow-up (LTFU) and pathways to health care before TB diagnosis of presumptive TB patients during an intervention study on intensified case finding at pharmacies.

Methods: Semi-structured explanatory model interviews, (EMIC) were administered to 70 presumptive TB patients who visited the pharmacies, consecutively enrolled and referred to a TB clinic in Dar es Salaam, Tanzania. We assessed patterns of distress, perceived causes and help-seeking behavior. We defined LTFU as presumptive TB patients who had not appeared at the TB clinic two months after referral from the pharmacy. Diagnostic delay was defined as three weeks or more after onset of symptoms. We used logistic regression models to identify patient factors associated with diagnostic delay and LTFU.

Results: The median age was 32 (interquartile range [IQR] 26-39). The median delay in seeking health care to the pharmacies after onset of symptoms was 14 days. Women were more likely to delay in seeking care (OR 3.8, 95%CI 1.2-11.9, $P = 0.02$) and more likely to be LTFU compared to men (OR 3.6, 95%CI 1.3-9.8, $P = 0.01$). Age and education level were not significantly associated with diagnostic delay or LTFU. The majority (36%) perceived dust as a major cause of TB (Figure): 'My working environment is full of dust; I think this is what caused me to have symptoms of TB.' Coughing was reported as a priority symptom (90%), followed by fever (60%).

Conclusion: Diagnostic delay and LTFU were associated with female gender among presumptive TB patients. These findings highlight the importance of gender as a determinant of timely diagnosis, the need to improve awareness for TB and access to care for women.

Figure Perceived causes of symptoms for TB



ORAL ABSTRACT SESSIONS

01. Resistance to TB drugs: new moves and what next?

OA-300-27 Ethical and political challenges related to new and emerging TB drugs and diagnostics

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Background: The introduction of new tuberculosis drugs (e.g., bedaquiline) and diagnostics (e.g., Xpert® MTB/RIF into existing TB programs raises a host of ethics challenges, including balancing the risks and benefits of introducing these new technologies. The goal of this project is to empirically describe these challenges and provide ethically sound and practical recommendations.

Methods: Semi-structured qualitative interviews were conducted with healthcare workers, advocates, and policy makers working in TB care. Interviews lasted approximately one hour, were audio recorded, then transcribed using NVivo 11. The research team collectively analysed interviews using Braun and Clarke's thematic analysis. To ensure consistency, a shared codebook was developed through coding and discussing the first three interviews. After developing the codebook, researchers coded the remaining interviews independently and met regularly to discuss themes and discrepancies to maintain consistency.

Results: One of the characteristic challenges faced by the TB community in balancing risk and benefits is the tension between limited availability of data concerning new interventions, while ensuring those greatest in need can access new diagnostics and drugs. Respondents revealed that TB programs are misguided to delay

implementation of new diagnostics on the basis of concerns about the ethics of diagnosing patients without available treatment. Interviewees expressed concerns that current TB research studies perpetuate inequalities and further marginalise already vulnerable groups. There is consensus that development and implementation of rapid diagnostics and new drugs cannot operate in isolation of the socioeconomic and political conditions of high-burden countries and vulnerable populations.

Conclusions: Conversations on the ethics of adopting new TB drugs and diagnostics need to be inclusive of the complex socioeconomic and political conditions of high-burden countries and vulnerable populations. It is clear that the development of new diagnostics and drugs has been long overdue. Moving forward, we need to better understand patients migrating for access to better treatment, clear regulations and action on compassionate use programmes for new drugs, and further training and strengthening of health systems in high burden countries for effective implementation of new diagnostics and drugs, with an eye towards meeting the SDGs and the goals of the End TB Strategy.

OA-301-27 Are time to positivity and the molecular bacterial load assay telling us a different story in a mouse tuberculosis model?

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Background: The mycobacterial population within tuberculosis (TB) patients is considered to be heterogeneous; several subpopulations of bacteria have been identified in different microenvironments. Environmental stress and antibiotic pressure can drive *Mycobacterium tuberculosis* into a non-replicating state. Current methods to monitor treatment response such as sputum smear or sputum serial colony counting have their drawbacks, it is unlikely that all subpopulations of *M. tuberculosis* are detected using these methods. Therefore more research and new techniques are necessary to provide more information about the different subpopulations.

Methods: We compared matched lung samples of our murine TB model, Colony Forming Unit (CFU) counting on solid media, Time To Positivity (TTP) using the Bactec MGIT 960 and the Molecular Bacterial Load (MBL) assay which determine the presence of mycobacterial 16S rRNA. Mice were treated for 24 weeks and treatment arms were designed as follows: Isoniazid (H) - Rifampicin (R) - Pyrazinamide (Z), HRZ-Streptomycin (S), HRZ - Ethambutol (E) or ZES.

Results: Our study revealed inverse correlations between TTP with CFU and MBL and positive associations between CFU and MBL. Description of the net elimination of bacteria was performed for CFU vs. time, MBL vs. time and 1/TTP vs. time during treatment with mathematical models (fitted by nonlinear regression). CFU vs.

time and 1/TTP vs. time showed bi-phasic declines with the exception of HRZE. A similar rank order, based on the initial elimination rate (alpha slope), was found comparing CFU vs. time and TTP vs. time, respectively HRZE, HRZ, HRZS and ZES. In contrast, MBL vs. time showed a mono-exponential decline with a relatively flat gradient of elimination and a different rank order respectively, ZES, HRZ, HRZE and HRZS.

Conclusions: We conclude that the correlations between methods reflecting the ability of each to discern a general load of *M. tuberculosis*. Based on the description of net elimination, we conclude that the MBL assay tells 'a different story' in a mouse TB model to that of CFU counts and TTP, by detecting a subpopulation of Mtb which is not detected by CFU or TTP assays and indicating a slower general elimination of the total bacterial load.

OA-302-27 Transcriptional analysis of genes associated with rapid acquisition of multidrug resistance in *Mycobacterium tuberculosis*

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Background: Though molecular basis for drug resistance in *Mycobacterium tuberculosis* has been attributed largely to mutations in drug-target genes, rapid accumulation of multi-drug resistance (MDR) in treatment compliant patients can be explained through alternate mechanisms for acquisition of drug resistance. Our earlier work on global transcription analysis of longitudinal clinical isolates showed deregulation of various multidrug resistance genes, efflux pumps, cellular metabolism and DNA repair. The study provided significant candidate genes indicating novel drug resistance mechanisms that could play a significant role in increasing fitness of low-level drug resistant cells and assist in survival of *M. tuberculosis* till better fit drug target mutants are selected. This study aims to validate and examine the deregulation of critical genes associated with drug resistance acquisition in vitro generated MDR strain from drug sensitive (DS) H37Rv strain.

Methods: Mono resistant and MDR H37Rv was generated in vitro through selection on Rifampicin (RIF) and Isoniazid (INH) containing media. Expression of 14 genes that were significantly associated with resistance acquisition in the microarray study was studied by qRT-PCR in both mono resistant and MDR H37Rv and was compared to DS-H37Rv. Statistical analysis for significance was carried out using t-test.

Results: Preliminary results show that of the 14 genes that were studied, *ddlA*, *ddlB*, *recB*, *recR*, *uvrB*, *ppsD*, *embC*, *ligA* were significantly ($P < 0.05$) upregulated and *whiB1* was significantly downregulated compared to DS-H37Rv only upon exposure to RIF. In absence of RIF, the levels of *ddlB*, *recR*, *uvrB*, *embC*, *ligA* and *whiB1* was comparable to DS-H37Rv suggesting their role in contributing to drug resistance in Mtb. In presence of INH, *recB*, *sigM* and *Rv1687c* was significantly ($P <$

0.05) upregulated. However, in absence of INH, the levels of *sigM* and *Rv1687c* decreased to levels comparable to DS-H37Rv suggesting their role in INH induced resistance.

Conclusions: Initial results show that genes belonging to DNA repair, cell wall synthesis and transporters are significantly deregulated upon exposure to drugs as observed in earlier microarray study. However, further research is in progress to exactly delineate the mechanisms contributing to drug resistance prior to development of stable mutants.

OA-303-27 Role of efflux pumps in conferring resistance in extensively drug-resistant *Mycobacterium tuberculosis* strains

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Background: The extensively drug-resistant tuberculosis (XDR-TB) has emerged as a major public health concern. XDR-TB is defined as TB caused by *Mycobacterium tuberculosis* resistant to least rifampin (RIF) and isoniazid (INH) among the first-line anti-TB drugs, fluoroquinolones and to at least one injectable aminoglycoside. Resistance in *M. tuberculosis* is associated with single nucleotide polymorphisms (SNPs) in particular genes but not all phenotypic resistance can be explained by non-synonymous mutation (nsSNPs). Efflux pumps facilitate additional resistance in MTB and up-regulation of these pumps can decrease the intracellular concentration of drugs. SNPs in efflux pump genes, *Rv0194*, *Rv2688c*, *Rv1634*, *rra* and *rrb* have been associated with drug resistance. We examined whole genome sequence data of XDR- *M. tuberculosis* strains and associated SNPs in these efflux pump genes with their transcriptional activity.

Methods: We studied XDR-TB ($n = 9$) strains characterised by WGS, (<http://www.ebi.ac.uk/ena/data/view/PRJEB7798>). Phenotypic susceptibility was performed by MGIT method. All XDR *M. tuberculosis* strains were resistant to at least 7 drugs whilst one was resistant to all 10 drugs tested including Streptomycin, Capreomycin and Ethambutol. SNPs in efflux genes and mRNA expression of genes; *Rv0194*, *Rv2688c*, *Rv1634*, *rra* and *rrb* was determined in XDR-TB as compared with the H37Rv reference strains using the relative quantification method normalized to 16S rRNA.

Results: A nsSNPs (Asp to His) in the *rra* at +32731382 in 2 strains. Two strains had nsSNPs (Ile to Val) in the Major facilitator superfamily (MFS), *Rv1634* efflux pump gene at +1839306. No nsSNPs in *Rv0194*, *Rv2688c*, *Rv1634*, *rra* or *rrb* were observed in other 5 XDR MTB strains.

mRNA expression studies determined that transcriptional upregulation of *Rv0194*, *Rv2688c*, *Rv1634* and *rra* was upregulated, whilst expression of *rrb* was reduced in all 9 XDR strains as compared with H37Rv.

Conclusions: Our data reveals that WGS data on SNPs in efflux pump genes may explain alternate mechanisms of resistance in *M. tuberculosis* strains. However, increased drug resistance in XDR-TB strains can be associated upregulation of efflux pump genes in the absence of SNPs in the same genes. Therefore, transcriptome data is required to fully understand the phenotypic resistance of *M. tuberculosis* strains.

OA-304-27 Evaluation of the Genoscholar FQ+KM-TB II (NIPRO, Japan) for detection of resistance to fluoroquinolones and second-line injectables

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Background: Line-probe assays (LPAs) have been endorsed by the World Health Organization for the rapid detection of drug-resistance to first-line drugs, while evidence was considered insufficient to endorse second-line drug LPAs. In this study, we evaluated the performance of the Genoscholar-FQ+KM-TB II (NIPRO, Japan) for detection of resistance to fluoroquinolones (FQs) and second-line injectables (SLID), hereafter referred to as FQ-LPA and KM-LPA respectively.

Methods: To evaluate the genetic performance, LPA results were compared to *gyrA*, *rrs* and *eis* promoter sequences as obtained by Sanger sequencing on a selection of 72 *M. tuberculosis* isolates from the research collection of the Institute of Tropical Medicine (Antwerp, Belgium). The overall performance was evaluated against a composite reference (sequencing and phenotypic DST). Phenotypic DST was done on 7H11 agar medium at 2 µg/ml (ofloxacin) and 6 µg/ml (kanamycin, KM).

Results: Classifying 74Ser and the double *gyrA* mutation 80Ala and 90Gly as not associated with FQ resistance, the genetic performance of the FQ-LPA is 97.2%, while the overall performance of the assay against FQ resistance by phenotypic DST and/or *gyrAB* mutations reached 88.2% (60/68). The positive and negative predictive values were 100% (39/39) and 75% (21/29) respectively. FQ-heteroresistant isolates were correctly identified.

Considering mutations a1138c and t1208g as not associated with KM resistance, the KM-LPA showed 100% concordance with target sequencing of the *rrs* gene and *eis* promoter. Seven of 11 *eis* mutants were found phenotypically susceptible to KM in our study (4 g-10a, 2 -14 and 1 -12). However, given the uncertainty about the true contribution of the *eis* mutations in to kanamycin resistance, our study can confirm 100% genotypic concordance of the KM-LPA, yet does not allow to draw firm conclusions on the performance against phenotypic DST.

Conclusion: The Genoscholar-FQ+KM-TB II showed excellent concordance with Sanger sequence. Overall

performance of the assay against FQ resistance by phenotypic DST and/or *gyrAB* mutations was as expected, while our study does not allow to draw firm conclusions on the KM-LPA performance against phenotypic DST.

OA-305-27 Performance characteristics of Abbott RealTime-MTB and RealTime INH/RIF-Resistance assays for direct detection of *M. tuberculosis* and genetic resistance markers

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Background: Abbott RealTime MTB (RT MTB) is a new commercial automated nucleic acid amplification-based test for the detection of *Mycobacterium tuberculosis* complex (MTBC) in clinical specimens. In combination with the Abbott RealTime MTB INH/RIF Resistance (MTB INH/RIF) assay, which can be applied to RT MTB positive specimens in a reflex mode, the tests also indicate genetic markers of resistance to isoniazid and rifampicin. We aimed to evaluate the diagnostic sensitivity and specificity of both assays and to compare performance characteristics with respiratory and extra-pulmonary specimens.

Methods: A total of 715 pre-characterized clinical specimens (412 culture negative specimens, 50 specimens growing non-tuberculous mycobacteria [NTM], 85 smear-negative and 168 smear-positive specimens growing MTBC) were retrospectively analyzed using RT MTB. Positive samples were analyzed in a reflex mode with the MTB INH/RIF assay.

Results: Based on culture as method of comparison, the overall sensitivity of RT MTB was 92.1%; the sensitivities for smear-positive and smear-negative samples were 100% and 76.4%, respectively. Sensitivity rates for smear-negative specimens were almost identical for respiratory (46/60; 76.6%) and extra-pulmonary (19/25; 76%) specimens. RT MTB showed 100% (412/412) specificity with culture negative specimens and 96% (48/50) specificity with specimens which grew NTM. RT MTB INH/RIF was applied to all 235 samples which were positive with RT MTB and yielded 189 (80.4%) valid results. Resistance pattern were not reported for 46 (19.6%) samples due to signals below the limit of detection. The RT MTB INH/RIF assay identified ten (4.3%) cases with multi-drug resistance, eight (3.4%) with isoniazid resistance and 171 (72.7%) with no resistance markers for isoniazid or rifampicin. Concordance with resistance patterns obtained by Genotype MTB-DR^{plus} (HAIN Lifescience, Germany) and phenotypic drug susceptibility testing in MGIT was 100%.

Conclusions: The RT MTB is a specific and sensitive assay for the diagnosis of TB. The RT MTB INH/RIF enables rapid and accurate testing for resistance markers in a reflex mode provided a sufficient amount of target DNA is present in the sample material.

OA-306-27 Different sensitivities of rapid phenotypic and genotypic methods for low-level rifampicin resistance conferring *rpoB* mutations

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Background: Rifampicin-resistant tuberculosis was diagnosed by phenotypic drug susceptibility testing (DST) until WHO approval of molecular methods, revealing discordant results, especially for 'disputed mutations' in the *rpoB* gene, responsible for low-level rifampicin resistance yet poor clinical outcome. We aimed at evaluating the capacity of the rapid phenotypic and genotypic methods to detect 'disputed mutants'.

Methods: A panel of 39 *Mycobacterium tuberculosis* isolates harboring 'disputed mutants', 5 with the *rpoB*531 mutation (positive control) and 15 wildtype strains were tested in MGIT960 (at 0.125, 0.25, 0.5 and 1.0 µg/ml with routine and extended incubation time), Nitrate Reductase Assay (NRA), Resazurin Microtiter Assay (REMA), Thin Layer Agar (TLA), Microscopic Observation Drug Susceptibility Assay (MODS, Sensititre (TREK Diagnostics), Genotype MTB-DR^{plus} V2 and Xpert MTB/RIF. We calculated the accuracy of the tests, including whether lowering the critical concentration and/or extended incubation time in MGIT960 could increase its sensitivity. Two different lots of the Genotype MTB-DR^{plus} V2 were evaluated in their ability to detect *rpoB* WT8.

Results: MODS and NRA detected >50% of disputed mutants with good specificity (92.3% and 100%). Mutant 511Pro was hardly detectable by any phenotypic method, while the remaining mutants were ≥50% detected by MODS and NRA, including mutation 572Phe not covered in genotypic methods. Concordance between MTB-DR^{plus} (74.4% detection rate) and Xpert MTB/RIF (79.5% detection rate) was 96.5% due to 2 false susceptible Genotype MTB-DR^{plus} results (511Pro). Mutation 533Pro (absence of WT8) was detected by the newest lot of Genotype MTB-DR^{plus}. MGIT extension to 21 days at the critical concentration increased its sensitivity without affecting specificity.

Conclusion: Genotypic methods perform well for the region covered, with Xpert MTB/RIF being slightly more sensitive than Genotype MTB-DR^{plus} V2 for mutation 511Pro. None of the phenotypic methods can detect all 'disputed mutants'. MGIT960 at 21 days of incubation detects mutation 572Phe not covered in molecular DSTs.

OA-307-27 Evaluation of access to drug susceptibility testing for previously treated tuberculosis patients in Botswana, 2013–2014

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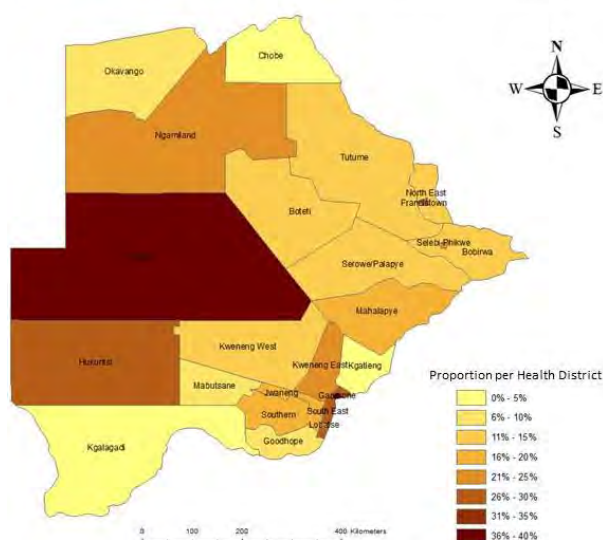
Background: WHO and Botswana tuberculosis (TB) guidelines recommend drug susceptibility testing (DST) for previously treated TB patients. The 2009 drug resistance survey in Botswana reported 6.6% of previously treated TB patients had multidrug resistant (MDR-TB); case-finding is thought to be suboptimal. Botswana has implemented Xpert MTB/RIF (Xpert) and is moving to universal access; currently, culture-based DST is still recommended. The National TB Reference Laboratory (NTRL) is the only culture facility in Botswana.

Methods: We evaluated access to DST, defined as the proportion of patients with at least one specimen submitted for testing. All previously treated, registered TB cases 1/2013–10/2014 were extracted from the TB registry and matched against NTRL records by unique identifiers. Specimens were tested using culture-based DST or Line Probe Assay for isoniazid and rifampin.

Results: Among 13 423 registered TB patients, 2072 (15%) were previously treated; 1110 (54%) submitted a specimen for culture. Only 459/1110 (41%) patients had at least one culture positive for *Mycobacterium tuberculosis*, and 415/459 (90%) had a DST result. Overall, 415/2072 (20%) previously treated patients had a DST result available; MDR-TB was identified among 43/2072 (2%). The proportion of patients with specimens submitted ranged from 19–85%, and the proportion with DST results ranged from 0–37% per health district (Figure).

Conclusions: Access to DST among previously treated TB patients varies considerably by health district. The proportion of patients with a DST result is low. Two major gaps resulting in missed opportunities to diagnose MDR-TB were identified: failure to submit specimens and low culture positivity. Low culture positivity could be due to a range of factors, under investigation, including specimen quality and poor transport. Program supervision and monitoring are needed to ensure guidelines are followed consistently. Greater access to Xpert through decentralized laboratories has the potential to reduce gaps and improve MDR-TB case detection.

Figure 1:
Proportion of Previously Treated TB Patients with DST Results Available, 2013–2014*



* NTRL closed for renovations in 11/2014; results were available through 10/2014.

02. Advocacy and community engagement

OA-308-27 Finding the missing 20%: active TB case finding through engagement of private health care providers in Mombasa County, Kenya

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Background: Tuberculosis remains a public health challenge post-2015 in developing countries. Worldwide in 2014, World Health Organization (WHO) estimated that about 9 million people developed TB. Kenya is ranked 15th among the 22 high TB burden countries which contribute 80% of the global TB burden. In 2014, over 89 000 TB cases were notified to the national TB programme (NTP) in Kenya. Mombasa notified 4726 TB cases giving a TB case notification rate of 469 per 100 000 that is above the national average of 208 per 100 000. From the cases notified less than 20% were from the private sector. The WHO estimates that 20% of annual estimates are still not being notified. Some of those missed are those who present to private providers and somehow diagnosis is missed. To get the missing cases Amref through support of the Global Fund contracted one civil society organization (CSO) the Kenya Association for the Prevention of Tuberculosis and Lung Diseases (KAPTLD) to coordinate TB active case finding (ACF) through engagement of private providers

Intervention: From April 2014 to December 2015, KAPTLD engaged private health care providers in Mombasa. The private providers were mapped to create linkages of referral and diagnosis. Sensitization was done

on TB symptomatic screening and referral. Government TB contact tracing, screening and referral forms were provided. Private providers referred all presumptive TB patients to link diagnostic facilities for TB diagnosis. Those diagnosed with TB were registered and started on treatment. Community health Volunteers were employed to follow up on referrals.

Results: Of the 738 private providers mapped, 281(38%) were engaged. In total 908 presumptive TB patients were referred for diagnosis out of which 487 (54%) arrived for diagnosis. Of those who arrived 124 (25%) were diagnosed with TB.

Conclusion: Engagement of private providers is crucial in TB active case finding in order to narrow the gap of the missed cases. Engagement of private providers to refer presumptive TB suspects is an innovative approach that can be scaled up for TB case finding

OA-309-27 Effective use of corporate social responsibility strategies to accelerate TB control in Mumbai, India

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Background and challenges to implementation: TB is a major public health challenge in Mumbai. Drug-resistant TB remains a cause for concern with ~3000 cases detected in 2015. Despite the government providing free diagnosis and treatment, challenges such as malnutrition, lack of quality infection control and awareness were identified. To address these concerns, the Municipal Corporation of Greater Mumbai (MCGM) devised and deployed several innovative fundraising strategies in 2014 and 2015–2016. The beneficiaries included drug-resistant TB patients.

Intervention or response: A needs assessment was conducted following which priority areas were selected: nutrition, demand creation, supporting diagnosis and infection control. Corporate partnerships and donations were sought for each priority area and deployed as required. Data was collected ward-wise by designated medical officers to understand the efficacy of each of the interventions.

Results and lessons learnt: An achievement of the corporate social responsibility (CSR) strategy was that several corporates and independent donors partnered the MCGM and crucial interventions were supported. Total funds raised in Mumbai via CSR till March 2016 was ~ USD 180 136 in cash and ~ USD 109 273 in kind. For example, the daily meal program reached over 600 patients per year; family nutrition packs were provided to 60 patients' families per month for one year; pediatric nutrition packs were provided to 100 patients for a year and 10 000 N-95 masks were provided to health care providers in Sewri TB hospital among other support. A case study was developed for assessing the impact of the pediatric nutrition support program which showed a

positive impact on treatment adherence and weight of the pediatric TB patients. Developing an efficient mechanism for the City government to accept CSR monies may help further increase CSR investments from corporates.

Conclusions and key recommendations: India's CSR law requires corporate houses turning revenue of 5 billion INR (USD 74 million) or more to allocate 2% of the average net profits of the previous 3 years towards a social cause. Since a large pool of resources through CSR is available, the same can effectively be channeled towards important public health concerns, especially in socially and economically vulnerable communities.

OA-310-27 From their own perspective: community perceptions of tuberculosis in a rural district of Eastern Tigray, Northern Ethiopia

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Background: Despite the availability of effective treatment for many decades, TB remains to be one of the few major killer diseases in the world. Studies reveal that TB persists in developing countries and among the socially disadvantaged community members. Many social science studies identified that the confusion of TB symptoms with other illnesses may affect health care choice. Therefore, it is important to recognize how TB is conceptualized by layperson and factors influencing such a perception. There is little knowledge on how TB is viewed and conceptualized in relation to other illnesses. Therefore this study explores the conceptions of TB from the perspectives of Tigray and Afar ethnic communities.

Method: The study was conducted in high TB prevalent region of Ethiopia. Qualitative methods of data collection (key informant interviews and focus group discussions (FGD)) were used to collect data from six purposefully selected sub-districts. A total of 12 FGDs (male and female community group separately) and 10 key informant interviews (health workers traditional healers and community leaders) were conducted. Preliminary content analysis and semiotic approach are used to describe the following themes: 1) TB as a biomedical disease; 2) *Qurilgala'o* [lit. cold in Tigrigna and Afar languages]/TB complex

Findings: The illness category *qurilgalao* covers variety of conditions including common cold, TB and folk illnesses not related to the respiratory system. Causation beliefs include being exposed to draft/wind, fatigue due to excess labor work, and social causes like migration. Many identify TB with *qurilgalao*, while most perceive *qurilgalao* can transform into TB. Most found *qurilgalao* is non communicable, while TB is contagious. Health seeking behavior is influenced by household economy and perceptions of causation and severity of illness.

Conclusion: TB may be confused with folk illnesses known as *qurilgalao*. Wide use of the term *qurilgalao* may affect decisions to seek a home based remedy or self treatment. The TB control program, including, educational activities, must consider how the communities in Tigray interpret the disease and vague terminologies like *qurilgalao*.

OA-311-27 Addressing TB vulnerability among the seven indigenous tribes of Bukidnon Province, Philippines

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Background and challenges to implementation: Bukidnon is home to seven indigenous tribes that comprise 40% of the province's 1.4 million population. Poverty, limited education, geographic and cultural barriers, as well as poor access to diagnosis, treatment, and care render them vulnerable to a host of health challenges, including tuberculosis. This points to the need for partners familiar with the characteristics and culture of indigenous communities, who come from the indigenous peoples' (IPs) village, and who can educate them on health in a language the IPs understand. To protect the rights of IPs, the national government has promulgated a law that provides for the mandatory representation of indigenous cultural communities in local legislative councils and policymaking bodies.

Interventions or response: With USAID technical assistance, the Provincial Health Office in coordination with the National Commission on Indigenous Peoples and the Department of Health Regional Office X engaged 216 municipal IP mandatory representatives (IPMRs) and oriented them on the TB disease, the national TB control program, as well as how to identify TB presumptive individuals and refer them to the nearest health facility for diagnosis and treatment. The PHO also established a referral mechanism between peripheral health centers and the IP office. The IPMRs then went out to the communities to educate the IPs and refer those with TB symptoms. Monitoring allowed the PHO to track the performance of the IPMRs.

Results and lessons learnt: In three quarters of engagement in 2015, six IP mandatory representatives who held TB education sessions with and referred TB presumptive cases from six *barangays* (villages, population: 17 002) in two towns contributed 10% (30/317) to the total notified cases of the said municipalities. Two of the TB patients had completed treatment and were cured while the rest are undergoing treatment. Similar case-finding activities are being conducted in the other municipalities of Bukidnon.

Conclusion: With proper training on TB education and identifying and referring TB presumptive cases to the nearest health center, mandatory representatives of indigenous peoples tasked to participate in local legislation and decision making can effectively contribute to improving case finding in IP communities.

OA-312-27 Reaching the hard to reach: finding the missing cases

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Background and challenges to implementation: Cambodia is one of the 22 countries with a high burden of tuberculosis (TB). The prevalence, incidence and mortality rates of TB in 2015 were 764, 411, and 63 per 100 000 population, respectively. Approximately 80% of the population is registered as rural dwellers, with a significantly high TB prevalence rate. Further, data show that in operational districts with a high proportion of household poverty rates, there are significantly low smear positive TB case notification rates, all consistent with poor access to TB care, high costs associated with seeking healthcare and low awareness about TB.

Intervention or response: Our TB project in Cambodia mobilized a Village Health Support Group (VHSG) to implement comprehensive interventions using an integrated approach to identify 'missing cases' in pagodas/mosques and congregate settings by involving religious laymen (ajar) and imams as supporters in TB control. During holy days, it is common for the elderly and ajar to visit pagodas or mosques for praying. TB posters are displayed at pagoda to promote TB awareness and inform about VHSG's contact information for TB services. Health Center staff and VHSG go to pagodas/mosques and set up discrete, private areas where individuals with one of multiple TB symptoms can be evaluated. Presumptive TB patients have sputum collected on site and sent to a local laboratory for GeneXpert test. Strongly presumptive TB cases with a negative result from GeneXpert are sent to referral hospital for x-ray and further work up. Transportation support is provided to the poor.

Results and lessons learnt: Within six months of implementation, TB symptom screening was conducted in 95 pagoda. 3452 elderly people were screened for TB and 41 TB case notification have been identified (1,187/100 000 screening population) which is quadruple higher than general population (291/100 000). Monks/religious men provided TB education to the community and the awareness of TB in the community increased.

Conclusions and key recommendations: Our targeted approach in pagodas/mosques provides a higher yield of TB case notification compared to routine TB service and if routinely integrated into the existing healthcare structure could significantly impact the elderly, a highly impacted, and neglected population.

OA-313-27 Engagement of public figures as catalysts for change

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Background and challenges to implementation: Given the high burden of TB (WHO Global TB Report 2015) in India, the country needs to lead with bold policies, patient centered care and support, coupled with intensified research and innovation for TB. A high level advocacy campaign, led by influential public figures, will have a multiplier effect and galvanize action to end TB. This paper evaluates contribution of public figures in efforts to mobilize domestic commitments for TB.

Intervention or response: Online media reports (English) (1 January, 2015–28 December, 2015) and print media reports (1 October, 2015–26 December, 2015) were analyzed using select keywords related to TB and Call to Action. A total of 1404 English reports were analyzed (1321 online; 83 print). Primarily, the trends from reports were analyzed by placement, publication, type of report, region, issues highlighted along with quotes from public figures and eminent personalities. Bi-variate analysis was carried to understand the media buzz on TB (when attended/quoted/ endorsed by public figures) vis-a-vis media reports without them.

Results and lessons learnt: On evaluating the media data above, spikes of high reporting were found in the months wherein public figures appeared/ endorsed/spoke about TB. These included launch of mission TB-Free Haryana by Dr Naresh Trehan, Mr Amitabh Bachchan, a famous Bollywood celebrity, US ambassador Richard Verma at corporate dialogue; Anurag Thakur, parliamentarian; P.J. Kurien, deputy chairman, Rajya Sabha and others; Sri Ratan Tata, famous Indian industrialist.

Conclusions and key recommendations: High media coverage of events/causes endorsed by eminent public figures reaffirms our belief that active engagement with opinion leaders from different stakeholder groups leads to increased visibility of the issue of TB and mobilizes domestic commitment. Due to celebrities' public presence, access to media platforms, and the admiration people often have for them, their personal connect and support of a cause also inspires action. Their spheres of influence can be leveraged to address advocacy bottlenecks and their collective effect can amplify efforts towards a TB-Free India.

Engaging public figures in advocacy and communication campaign efforts increases media visibility and reporting on issues that need more public health focus.

OA-314-27 The TB Forum: building coalitions for evidence-based parliamentary advocacy to end TB

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Background and challenges to implementation: The Western Pacific region reports 1.6 million cases of TB per annum, which is approximately one sixth of the global TB burden. Australia, a low TB burden country, is surrounded by countries with high burdens of both drug sensitive and drug resistant TB. Despite this, TB does not have a high profile in Australia. A number of Australians have worked on TB prevention and care for many decades. However, such efforts were often in isolation without strong inter-disciplinary partnerships to effect political change.

Intervention or response: In 2014, a coalition of public health professionals, advocates, researchers, medical professionals and people affected by TB launched the TB Forum. The TB Forum had three broad advocacy goals: engage MPs, engage the community, and advocate for strong evidence based policies in the Asia-Pacific region. Prior to the establishment of the TB Forum, partners had very little exposure to each other's work and there were differences in opinion on the direction of policy. To resolve this, partners used their respective skills to collaborate on activities designed to raise the profile of TB.

Results and lessons learnt: A strong collaborative approach contributed to successful engagement with MPs and other stakeholders. As a result, advocates have been able to tap into professional scientific advice, ensuring nuanced and evidence based policy proposals. Researchers and medical professionals have forged relationships with MPs, and are seen as a source of expert advice on TB. People affected by TB have joined political forums to bolster support for political engagement on TB. The media have become sensitised to the often-complex issues that TB presents.

Conclusions and key recommendations: Worldwide, people who work in TB often separate themselves from each other and have little in-depth appreciation of the work that other groups do. The TB Forum's great strength comes in its diversity, with the inclusion of a wide group of stakeholders, which allowed for robust policy debates and collaboration in a range of fora designed to promote political engagement around TB. We recommend the model of the TB Forum as an example that other countries can adopt.

OA-315-27 Importance of documentation and data management for advocacy: a case study of 'Call to Action for a TB-free India'

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Background: Despite years of the national TB-control programme, the TB burden in India continues to be highest (WHO Global TB report 2015); the prevalence rates have come down, but incidence is still high. Government alone cannot handle this problem without active support from stakeholders. Call to Action for a TB-free India was launched to create and sustain high-level domestic commitment to End TB. The learning from this project will empower other advocacy efforts and projects to understand which stakeholders have a huge role to play in achieving zero TB deaths, zero TB disease, Zero TB suffering. This paper outlines the role of documentation and data management in increasing effectiveness of the advocacy effort.

Intervention or response: Guided by a 'documentation and data management plan', a comprehensive database was prepared and updated for mapping of stakeholders, strategic outreach to them, information dissemination and continuous engagement. Minutes of the meetings, meeting notes, consultation reports, audio visual recordings, photographs and progress updates (in pre-approved templates) diligently captured the 'tacit knowledge'. Letters of correspondence, activity briefs, participant's lists & reports were collected, to support the M&E and Knowledge Management function of the project.

Results and lessons learnt: As a result of rigorous document and data management, the project was able to document planned vs. successful outreach with identified & mapped stakeholder. Well documented media coverage served as early indicators of increased visibility and projects success. Diligent filing of records helped capture M&E outputs and meet targets as per project plan. However, this is not without challenges of data collection, frequent Updation and maintaining confidentiality of sensitive data.

Conclusion and key recommendations: Sturdy documentation and record management plan increases effectiveness of an advocacy project and also facilitates evidence based outreach to potential stakeholders, including policy makers. The distilled learning helps in tapping the energy of multiple stakeholders and collective action towards achieving the goals of End-TB strategy.

03. Prisons, slums and the homeless

OA-316-27 Role of mass screening in uncovering outbreaks of TB in correctional settings

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Background: Namibia is a southern African country with a high estimated incidence of TB (561/100 000). The Namibian Correctional Service (NCS) is developing strategies for systematic screening of inmates on admission into the correctional facilities. Meanwhile, following a recommendation from the first mass screening campaign, a second campaign was conducted after 6 months to monitor the trends and better quantify the burden.

Intervention: Using experience and tools developed 6 months earlier, a simultaneous symptomatic screening was conducted in all correctional facilities, targeting correctional officers and inmates. Individuals from the target groups were asked about five key symptoms (presence of cough, night sweats, fever, weight loss, and swollen lymph nodes), as well as about HIV and other medical history. Any positive response on the symptoms was followed by sputum collection (two samples) and testing using smear microscopy and Xpert MTB/RIF.

Results: 12 correctional facilities participated, with 909 of 3343 (27%) inmates and 410 (21%) officers being screened. 265 (29%) inmates and 66 (16%) officers had symptoms, with all submitting sputum for testing, except 3 inmates. Six bacteriologically positive cases were noted among inmates and two among officers. Of note was that both TB cases among the officers and five (83%) of the cases among inmates were recorded in one of the 12 correctional facilities, Grootfontein. This campaign screened 75% of inmates and 21% of the officers in this one facility, while the initial campaign had covered 93% and 40% respectively. The initial campaign did not register any positive cases among both inmates and officers.

Conclusions: This second mass screening campaign, occurring six months after the first, had uncovered an outbreak of TB in Grootfontein Correctional Facility. The absence of any detected cases with a higher coverage in the earlier campaign confirms that this was a recent outbreak. Of note is that both inmates and officers were affected. Periodical mass screening for TB should be maintained in Namibia, in addition to mandatory admission and exit screening in order to detect such outbreaks. There is need to address sensitization and stigma reduction to motivate better participation in future campaigns

OA-317-27 Yield of systematic screening for tuberculosis among vulnerable populations using enhanced diagnostic tools and algorithms in Palawan, the Philippines

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Background: Tuberculosis (TB) case-finding project (DetecTB) using mobile unit equipped with digital X-ray machine, Light Emitting Diode Fluorescence Microscope (LED-FM) and GeneXpert machine has been implemented in Palawan, the Philippines, since 2012. The project organized the systematic screening for TB among vulnerable populations including prison inmates, indigenous populations, the urban and rural poor, and high school students. This study aimed to assess the yield of the systematic screening by different target populations.

Methods: All individuals aged ≥ 15 years underwent symptom screening and chest X-ray examination. Two sputum specimens were collected for sputum smear microscopy and Xpert MTB/RIF assay from TB suspects with symptoms suggestive of TB or abnormal X-ray findings. All bacteriologically confirmed cases and clinically diagnosed cases were referred to health facilities for treatment in line with national guidelines. We retrospectively reviewed the data on screening and treatment outcomes.

Results: A total of 25 115 participants were screened until August 2015. Of them, 5228 (20.8%) were identified as presumed TB, and 764 (3.0%) were diagnosed with TB. The yield of all forms of TB by each target group was 6.2% in prison inmates, 2.9% in indigenous populations, 2.2% in the urban and rural poor, and 0.2% in high school students. Treatment success rate (TSR) for rifampicin-susceptible TB, rifampicin-resistant TB and clinically diagnosed TB was 89.6%, 83.3% and 88%, respectively.

Conclusions: The systematic screening for TB targeting vulnerable populations with innovative diagnostics and algorithms could achieve remarkable results with good treatment outcomes. Further analysis is required to determine the cost-effectiveness of the project.

OA-318-27 Effectiveness of active TB case finding among prisoners in two prisons in Afghanistan

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Background: Based on Ministry of Interior statistics, there were almost 30 000 prisoners in Afghanistan in 2015, and screenings from 2011 revealed extremely high incidence of TB among prisoners compared to the general population. The National Tuberculosis Control Program (NTP) and partners initiated active TB case finding among prisoners in 8 provinces in 2011. Among 3000 prisoners, 233 (8%) were identified as presumptive TB cases, and 11 (5%) were bacteriologically confirmed TB patients. The objective of this study is to evaluate the role of new active case finding approaches (sputum smear microscopy and digital X-Ray) in prisons.

Intervention: Challenge TB began TB services provision on October 2014 in Pul-i-Charkhi prison in Kabul and Bigram prison in Parwan provinces with approximately 8945 prisoners. The intervention included:

- TB training for health care staff
- Establishing TB diagnostic and treatment centers in each prison
- Sputum smear microscopy and mobile digital X-Ray for diagnosis
- Patients isolated and treatment provided and monitored at months 2, 3, 4, and at end of treatment
- Standard Operation Procedure for prison and IEC materials developed and distributed
- Awareness activities to reduce stigma
- NTP and Challenge TB technical teams used standardized tools to collect, review, and analyze data from October 2014–December 2015 from both prisons.

Results: Among 8945 prisoners, 749 presumptive TB cases identified and referred to digital X-Ray and sputum smear microscopy, resulting in 179 clinically confirmed TB cases (2001/100 000 persons). This is much higher than the estimated incidence of TB in the general population (189/100 000). Among 749 presumptive TB cases, 126 (16.8%) were bacteriologically confirmed TB cases. 28 of 30 (93%) bacteriologically confirmed TB cases completed their treatment, a higher treatment success rate than 89% at national level.

Conclusion: Active TB service provision resulted in significant improvements in TB case detection and treatment completion rates among prisoners. We recommend scaling up TB services to all prisons in provinces.

OA-319-27 Role of systematic screening in improving tuberculosis case detection in selected urban slums of Bangladesh

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Background: Tuberculosis (TB) is still believed to be a disease of the poor. Overcrowding coupled with poor living conditions make slums highly vulnerable to TB. An estimated 150 000 cases are missed annually in Bangladesh and alternative case finding strategies are warranted to improve case detection in such high risk settings. The urban slum dwellers of Dhaka are mostly industrial workers and have poor access to DOTS centres due to inconvenient business hours. Very often this leads to delayed diagnosis and higher transmission of TB.

Methods: From January 2013 to June 2014, every household of Mirpur, Section-11 slum area, was visited once and the members were systematically screened for TB. Revisits were made to cover any absentee. People having cough for ≥ 2 weeks and/or Body Mass Index $< 17 \text{ kg/m}^2$ were identified as presumptive TB cases. Sputum samples were collected from them and were subjected to smear microscopy, culture and drug susceptibility testing (DST) in solid media. Xpert MTB/RIF (GXP) assay was performed on a subset of smear negative samples. For transmission analysis, we collected all additional samples from the smear positive patients of local DOTS facilities during this study period and performed spoligotyping and deletion analysis on those along with the samples from study patients.

Results: A total of 99 946 people were screened and 1928 (2%) presumptive TB cases identified. Sputum specimens were collected and tested in 695 (36% of 1928) presumptive cases and 134 (19%) TB cases were identified. GXP detected 17 (4.2%) cases among 409 smear negative samples tested. Case detection increased by 12% from the baseline. Among the cases, 78% were from productive age group (15–54 years) and the male to female ratio was 1.1:1. Four multidrug-resistant TB cases were identified. Majority (53%) of the strains was modern type and the largest cluster comprised of Beijing family with 19 (22%) strains.

Conclusions: Systematic screening at every household at least once a year should be implemented by the national program to increase TB diagnosis in urban slums. To confirm the evidence of transmission found in this study, large scale molecular epidemiological studies should be conducted in such settings.

OA-320-27 The impact of the Xpert® MTB/RIF assay in pulmonary tuberculosis case detection during house-to-house active case finding in urban slum dwellers

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Background and challenges to implementation: The 2012 National Tuberculosis (TB) prevalence survey revealed that only 15% of the estimated TB burden in Nigeria is detected annually and that most of the undetected cases remain within the communities. Because of this, and the global push to improve TB case-detection especially in low income countries, the implementation of evidence based active case finding (ACF) strategies became imperative. We aimed to assess the impact of these strategies on TB case detection among the urban slum dwellers in Kano, Northwestern Nigeria.

Intervention or response: From 13–20 September 2014 and 12–19 December 2015, the World Health Organization (WHO) and the National Tuberculosis Program (NTP) conducted a house-to-house TB ACF in three slums of Kano Metropolis. TB workers and community health volunteers performed symptom screening, collected sputum and facilitated specimen transport to the laboratories. Simple sputum microscopy was performed at three designated health facilities. The GeneXpert MTB/RIF assay (Xpert), which was not utilized in 2014, was introduced in the 2015 activity. TB workers contacted diagnosed patients and commenced them immediately on appropriate treatment at the nearest local health center.

Results and lessons learnt: In 2014, within one week that the activity lasted, a total of 24 035 individuals were screened for TB; 456 aged ≥ 15 years were identified as presumptive TB cases; all of them provided sputum and 5 were bacteriologically confirmed. In 2015, within the same duration, a total of 40 350 individuals were screened, of which 381 presumptive TB cases aged ≥ 15 years were identified and investigated, resulting in 9 bacteriologically confirmed cases and 7 additional Xpert diagnosed ones, making a total of 16 confirmed TB cases.

Conclusions and key recommendations: Our findings suggest that combining sputum AFB microscopy and Xpert test during house-to-house ACF intervention is capable of finding additional TB cases than when using sputum AFB microscopy test alone. Other benefits include improved case detection of both drug-susceptible and drug-resistant TB, shortening the diagnostic delay, and successfully bringing patients into treatment and care. The strategy is therefore highly recommended for National Tuberculosis Programs especially in low income countries.

OA-321-27 Computational modeling of TB epidemiology in Nigerian urban slum environments

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Background: Nigeria has the highest number of TB cases in sub-Saharan Africa. Urban slum residents, numbering as high as 50 million in Nigeria, have been identified as a key affected population in recent strategic planning. However, questions remain about TB epidemiology in urban slums including how quickly interventions could reduce TB burden in this setting given ongoing transmission, a high HIV burden, and other social and biological factors.

Methods: To understand the ongoing TB epidemic in urban slums, we developed a computational model of TB in urban slums in Nigeria based on national prevalence survey results and recent studies on active case-finding in health clinics in urban slums. Using an individual-based framework, the model explicitly represented three population groups in Nigeria (urban slum residents, urban non-slum residents, and rural area residents), mixing among these groups, risk factors such as HIV co-infection and mitigation by antiretroviral treatment, and DOTS and non-DOTS treatment options.

Results: The model reproduced several epidemiological indicators related to TB in Nigeria including the two-fold higher prevalence observed in urban vs. rural areas and the higher prevalence observed in slum vs. non-slum environments. However, the model showed that different factors could account for the higher burden in urban slums including higher transmission or reactivation rates. These uncertainties strongly determined the projected impact of urban slum-targeted interventions. In particular, active case-finding was more effective if a greater share of the burden was attributed to crowding and high transmission rates.

Conclusions: Depending on whether the high TB burden in urban slums in Nigeria is attributable to higher transmission or reactivation rates, the model predicts that interventions targeting urban slums will differ in their impacts. As these factors are measurable in principle, the model can be used to provide guidelines for future research studies which would in turn allow the impact of urban slum-targeted interventions to be estimated more precisely.

OA-322-27 Transmission events revealed in tuberculosis contact investigations in London, 2012–2014

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Background: Contact tracing is a key part of TB prevention and care in London. Information on its impact and effectiveness, however, is limited. We aimed to assess contact tracing by determining whether cases identified through tracing were part of the same chain of transmission as the index, and were identified sooner than the index.

Methods: We analysed TB contact tracing data from cohort reviews in London, from 1 January 2012 to 31 December 2014, linked to surveillance and strain typing information held by Public Health England. Pairs of index cases and contacts with active TB were included if both were culture positive. If the strain types (MIRU-VNTR 24 locus genotyping) isolated from both individuals were indistinguishable they were considered part of a transmission event. Those with differing strain types were considered unrelated. The median time interval between symptom onset and treatment start for all index cases and contacts was calculated.

Results: Of the 246 unique pairs of index cases and contacts diagnosed with TB, in 72 both index and contact were culture-positive. 65% (47/72) of these culture positive pairs shared identical isolates. When the index case and contact both had one or more social risk factor (history of imprisonment, drug use or homelessness) they were more likely to have indistinguishable strain types (82%, 18/22, $P = 0.04$). The median time interval between self-reported symptom onset and treatment start for 188 index cases with data available was 71 days (IQR 32.5–121); for 140 contacts with data available the median interval was 32 days (IQR 14–93.5).

Conclusions: Two-thirds of all contacts, and 82% of those with social risk factors, had isolates that were indistinguishable from that of their index case, suggesting that contact tracing in London is likely to be identifying transmission. Previous work has shown that contacts of index cases with social risk factors are less often evaluated than those without; improving contact tracing outcomes for this group may prevent a large number of transmission events. The shorter median time to diagnosis among cases identified through contact tracing compared to index cases demonstrates the importance of contact tracing to TB prevention and care.

OA-323-27 Tuberculosis contact tracing outcomes in London, 2012–2014

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Background: Contact tracing, which aims to hasten diagnosis and thus reduce transmission, is one of ten key elements in the Public Health England and NHS England collaborative tuberculosis strategy. The proposed indicators of successful contact tracing are not currently well-characterized in England. We aimed to describe current contact tracing outcomes in London, and identify characteristics associated with better outcomes.

Methods: We conducted descriptive, ecological & multivariable analyses of contact tracing outcomes of TB cases in London during 1 January 2012–31 December 2014 using cohort review data on close contacts from the PHE London TB Register. We compared contact tracing outcomes across London boroughs, and explored the clinical and demographic characteristics associated with contacts being identified and evaluated (for signs of TB and latent infection).

Results: Of the 3056 pulmonary TB cases notified, 2162 had sufficient information on contact tracing outcomes to be included. 91% (1963/2162) of pulmonary cases had at least one contact identified. A median of four contacts were identified per case. 86% (8272/9656) of contacts were evaluated. For pulmonary index cases, 3.6% (299/8272) of evaluated contacts had active disease and 12.9% (1067/8272) had latent infection. For index cases without pulmonary involvement 1.5% (88/5,729) of contacts had active disease and 5.9% (336/5729) had latent infection. Smear-positive index cases were more likely to have at least one contact identified (aOR 2.18, 95%CI 1.36–3.49) as were female index cases (aOR 1.82, 95%CI 1.22–2.69). Index cases with a prison history were less likely to have contacts identified (aOR 0.30, 95%CI 0.15–0.61). Contacts of female index cases were also more likely to be evaluated (aOR 1.40, (95%CI 1.10–1.78), as were contacts aged under 15 years (aOR 3.57, 95%CI 2.78–4.76)). The average number of contacts evaluated per clinic was moderately positively correlated with the average number with latent infection ($R^2 = 0.27$) or active TB ($R^2 = 0.14$).

Conclusions: These are the first London-wide estimates of contact tracing outcomes. While our main results compare favourably with previous data from London and similar countries, we found the effectiveness of contact tracing differs between groups. Further work to understand the reasons for these differences will help TB services improve contact tracing outcomes in these groups.

04. 'Here, there and everywhere': how to end TB

OA-324-27 The tuberculosis cascade of care in the Indian public sector: current estimates and gaps in knowledge

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Background: India has 24% of the global tuberculosis (TB) burden and 27% of the world's 'missing cases' patients who may not receive effective TB care. The 'cascade of care' is a useful model for visualizing deficiencies in case detection and patient retention in the Revised National TB Control Programme (RNTCP), which treats more than half of India's TB patients.

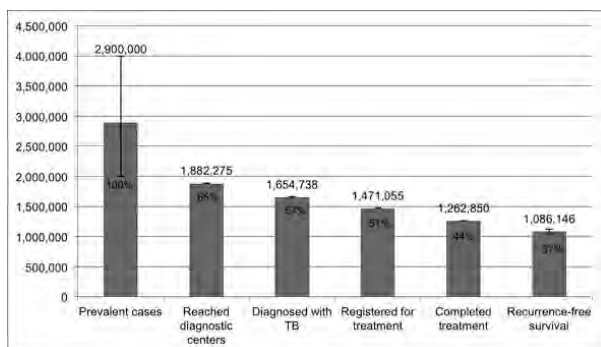
Methods: We define the TB cascade as including these patient populations: total prevalent cases in India, cases who reach RNTCP diagnostic services, cases diagnosed, cases who started treatment, cases retained to treatment completion, and cases who achieve one-year recurrence-free survival. We estimate cascade steps for 2012 using data from WHO and RNTCP reports and with three systematic reviews of >40 local studies published from 2000 to 2015.

Findings: The WHO estimates that there were 2 900 000 prevalent TB cases in India in 2012. We estimate that 1 882 275 (65%) TB patients were evaluated at RNTCP facilities; 1 654 738 (57%) were successfully diagnosed; 1 471 055 (51%) got registered in treatment; 1 262 850 (44%) achieved treatment completion; and 1 086 146 (37%) patients achieved the optimal outcome of one-year recurrence-free survival. Multidrug-resistant (MDR) TB cases had much poorer outcomes than other patient subpopulations, with <4% of prevalent MDR cases among notified TB cases in 2012 estimated to have achieved one-year recurrence-free survival.

Conclusions: Increased case detection is critical to improving the cascade's outcomes, especially for MDR-TB patients. For new smear-positive patients, pretreatment loss to follow-up and post-treatment relapse are considerable points of attrition. These gaps may contribute to TB transmission. In contrast, under-diagnosis of patients who reach RNTCP facilities is the major point of attrition in the smear-negative cascade. Future multi-site studies providing more accurate information on key cascade steps and on private sector outcomes may help to

refine the cascade and better target resources for TB control.

Figure Cascade of care for all forms of TB in India, 2012



OA-325-27 An assessment of the TB screening-to-treatment cascade in Swaziland

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Background: Swaziland has one of the highest incidence rates of TB in the world, estimated at 733 new infections per 100 000 people in 2014.¹ Clinical management of drug sensitive (DS) and drug resistant (DR) TB is compromised by high rates of patient loss to follow-up (LTFU). Clinton Health Access Initiative (CHAI) supported the Swaziland National TB Control Program (NTCP) in performing an assessment of the TB diagnosis-to-treatment cascade to identify leakages contributing to LTFU.

Methods: The assessment consisted of a national level data review and a facility level assessment. Eleven national level M&E and laboratory datasets were analyzed between December 2014 and May 2015 using Microsoft Excel. Aggregate data was compiled for patients screened in 2013, as this provided a full dataset for screening to treatment outcome. Facility surveys conducted in October 2015 included 63 healthcare facilities, 25 peripheral laboratories and the National TB Reference Laboratory. A paper-based questionnaire was administered to healthcare workers involved in clinical and laboratory management and data were analyzed using STATA.

Results: The analysis identified major gaps throughout the cascade:

- **Diagnosis:** GeneXpert MTB/RIF is used as the initial diagnostic test for only ~50% of the total DS-TB diagnoses and the current GeneXpert network distribution is sub-optimal.
- **Treatment enrollment:** less than 50% of the GeneXpert tests are followed up with culture & DST and 12% of

GeneXpert diagnosed RR-TB cases are not enrolled into treatment.

- **Patient management:** 64% of DS-TB treatment successes outcomes fail to prove sputum conversion and 30% of the MDR-TB patients are LTFU.
- **M&E systems:** Only 20% of all facilities report on TB screening, there is no use of a national unique identifier number data collection and management systems are not well coordinated.

Conclusions: The analysis has already led to changes in diagnostic guidelines and training programs for health-care workers and will result in improvements in M&E systems through the rollout of GeneXpert connectivity platforms, DR-TB surveillance systems and the consolidation of national databases. A cascade assessment allows NTPs to identify weaknesses at all levels across the TB cascade and help define the appropriate integrated and comprehensive response to those challenges.

Reference

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OA-326-27 Making sense of tuberculosis data: how district and facility staff can use their own routine data for management

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Background and challenges to implementation: Recording, reporting and supportive supervision were key components of the tuberculosis (TB) DOTS (directly observed treatment short course) strategy developed by the Union Against Tuberculosis and Lung Disease (The Union) in the 1980s and in the Stop TB strategy. However, recording and reporting is less visible in the End TB Strategy, although there has been increasing concern over quality of data. The aim of this paper is to present the impact on programme performance of districts piloting a new approach to strengthen district and facility level staff's use of their own routine TB data for management.

Interventions: The National TB Programme (NTP) of Zimbabwe developed the approach with The Union support from 2009 and piloted it in districts in 2012. A new facility quarterly report was introduced, including additional data from presumptive TB registers. A new NTP guide described the approach with key indicators on presumptive TB and MDR-TB, TB, TB/HIV, treatment outcome, DOT and drug management. Staff tabulated and analysed the data using these indicators to identify strengths and challenges and agreeing on action points. Supportive supervision was 'data-driven' using check-lists and guided by summary tables of routine data and similarly in performance review meetings. Routine data quality and program performance the year previous were compared with the year of

implementation and with corresponding changes in the province.

Results and lessons learnt: The district with full implementation of the approach showed 103% increase in new smear-positive TB cases (2% increase in province), 77% increase in presumptive TB cases (40% in province) and 77% decline in pulmonary TB cases without smear results (23% in province). NTP has since expanded the approach to the whole country.

Conclusion and key recommendations: The pilot data suggest that data quality and program performance have been strengthened. The new approach makes better use of routine TB data for management, promotes quick, simple and comprehensive on-site assessment of key TB program components and increases local staff motivation and ownership. NTPs and partners should promote the approach and also consider using it in other programs, contributing to strengthening the health systems and implementation of the End TB Strategy.

OA-327-27 Schedule H1 drugs status for anti-tuberculosis drugs an effective surrogate marker for TB case notification: an Indian case study

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Background and challenges to implementation: India accounts for a 'missing million' TB cases which get missed for notification. Government of India in 2012 has made TB case notification compulsory under the law. However the implementation remains suboptimal. Indira Gandhi Medical College and Hospital Shimla in Himachal Pradesh is one of the largest teaching hospitals in Northern India. Despite several sensitization activities in the institute, many doctors are reluctant to notify TB patient to health authorities, which amounts not only to violation of law but also barring the patients from availing the several supportive services being provided under National TB program to the notified patients.

Intervention or response: Government of India in 2013, under Drugs and Cosmetics Rules brought Anti TB drugs under Schedule H1 list, which mandate each chemist to record the sale and supply of these drugs in a separate register along with the name of prescribing doctor. Investigator in January 2016 extracted information from the entire five chemist shops in the hospital campus on a structured checklist with several key variables including amount of anti TB drugs sold between July 2015 and December 2015.

Results and lesson learnt: A total of 561 prescriptions have been recorded in these shops. Near one-fourth of prescriptions were of non-standardized regimen. Over prescriptions was noticed in near half of the slips. Investigator also cross checked the TB case notification records available with district health authority and triangulated with the records obtained from chemist shop. It was revealed that total 45 TB cases were notified during this duration and there exists a gap of 516

patients, which remain unnotified and is essentially a part of India's missing million TB patients' population.

Conclusions and key recommendations: TB case notification is poorly implemented, there is an urgent need to address this issue through an administrative control and sensitization of doctors however the monitoring schedule H1 provision proved to be an effective marker for assessing gaps in the TB notification. Strategic monitoring of schedule H1 provision gives an additional yield in TB case notification, provides information on existent prescription practice and an opportunity for initiating public health actions.

OA-328-27 Towards zero stock-outs of anti-tuberculosis drugs: focusing on system strengthening brought a difference in two regions of Ethiopia

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Background: Frequent stock out of anti-TB drugs at health facilities was one of the challenges that caused many patients to interrupt treatment and promoted drug resistance. Stock outs are often due to poor implementation of the pharmaceutical logistics management system along with weak inventory control management. We present our experience in achieving near zero anti-TB stock out rate in two regions of Ethiopia.

Intervention: The USAID funded Help Ethiopia Address the Low TB Performance (HEAL TB) project supported the Ministry of Health (MOH), Pharmaceuticals Fund and Supply Agency (PFSA), the Amhara and Oromia Regional Health Bureaus (RHBs), and health facilities in implementing an integrated pharmaceutical logistics system (IPLS) between December 2011 and September 2015. IPLS improves drug supply management through integrating drug requisition, distribution, and reporting into a single mechanism. A total of 3424 health care workers were trained on IPLS. The project distributed Standard Operating Procedures on IPLS as well as IPLS recording and reporting tools to all health facilities. District based quarterly TB program mentorship was provided one of the components being IPLS.

Results and lessons learnt: After implementing IPLS, a follow-up assessment conducted between July and September of 2015 showed that the anti-TB drug stock outs decreased by 89.1% as compared with the baseline. The presence of updated stock card and use of drug requisition and reporting forms increased by 212.4% and 747.3% respectively, after four years of intervention.

Conclusions: Implementation of IPLS and district based mentoring contributed to significant improvements in the anti-TB drug stock out rates in the Amhara and Oromia Regions of Ethiopia. This intervention should be expanded and replicated in other areas.

Table Improved TB drug supplies and management

Indicator	Baseline Oct - Dec 2011	End line July- Sept 2015	Percentage Change
Stock out adult anti-TB drugs	22%	2.4%	Decreased by 89.1%
Up-to-date stock cards	25%	78.1 %	Increased by 212.4%
Use of drug requisition and reporting forms	11%	93.2 %	Increased by 747.3%

OA-329-27 Sub-national rationalization of integrated HIV/AIDS/TB partners could mean increased funding for TB programs: a case for Uganda

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Background: Closing the funding gap for Uganda's National Tuberculosis and Leprosy Program remains a key challenge for the TB response. There is inadequate tracking of national TB program resources from different sources resulting in limited quantification of funded interventions to inform the national response. Against this background, the Government of Uganda and PEPFAR initiated a drive to rationalize sub-national partners where one partner supports implementation of HIV/AIDS/TB services in defined geographical areas and thus reduce duplication of efforts. As part of rationalization, PEPFAR subcontracted Makerere University Infectious Diseases Institute (IDI) to support a comprehensive HIV response in Buliisa, Hoima, Kibaale, Kiboga, Kiryandongo, Kyankwanzi and Masindi districts in Western Uganda. This paper describes strategies taken by IDI to attain efficiency gains while integrating TB services into HIV programming.

Intervention: In July 2015, as part of strengthening IDI's capacity to ably integrate TB, an HIV-TB advisor and four TB technical support officers were recruited to support TB response in the districts. Districts have been supported to develop and operationalize integrated HIV-TB strategic and annual plans. These officers have supported capacity building for health workers in provision of HIV-TB care, MDR-TB surveillance, logistics management, strategic information and laboratory strengthening. Performance in the above interventions is periodically tracked by the respective specialists at higher level of project management.

Results: Between August 2015 and March 2016, funds to achieve the TB program outputs registered in the region have been drawn from five cost areas: HIV-TB, adult HIV basic health care and support, adult antiretroviral services, strategic information and system strengthening. Only TB-HIV resources would be reported to the national TB program as contribution to TB program-

ming contrary to the five TB program cost areas whose interventions would have been funded in parallel. These include; TB-HIV, laboratory infrastructure, TB program staff, program costs for drug-susceptible TB and program costs for drug-resistant TB.

Conclusions: Rationalization of one comprehensive HIV partner in a geographical area results in efficiency gains for TB programming. More efficient gains could be quantified by improving tracking of resources from different funding sources.

OA-330-27 A technology-enabled social franchise approach to increase tuberculosis case detection and cure rates in urban Patna, Bihar, India

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Background and challenges to implementation: TB causes two deaths every three minutes in India. In Bihar, as many as 58 814 new TB cases surfaced in the year 2014. The focused of Government of Bihar (GoB) has been on diagnosing and treating TB and preventing new TB cases. Health Department, GoB has been working in collaboration with World Health Partners as Private Provider Interface Agency (PPIA) towards strengthening TB control efforts in urban Patna by engaging and networking with existing qualified and informally qualified providers, chemist shops and diagnostic facilities by using a technology-based reporting platform (ICT), and an inclusive system of financial and service incentives, to motivate appropriate delivery of TB diagnosis and treatment.

Intervention or response: The team works with qualified or informally qualified providers, chemist shops, and private sector diagnostic facilities to create networks to ensure patients receive appropriate care and referrals, including the latest diagnostic technologies and an e-voucher system for receiving subsidized TB drugs. The mechanism/process includes identification of presumptive TB cases; providing free/ subsidized diagnostic facilities; free anti-TB drugs; notification and treatment adherence tracking as well as other functionalities via ICT platform developed for the PPIA engagement; specimen transport and rapid results reporting.

Results and lessons learnt: The program metrics/intervention includes engagement of: doctors 658, informal providers 719, chemists 688, labs and X-ray units 148, which has resulted in PPIA notifications of 20 246 patients. The total 18 235 patients commenced on Free Drug where 8020 patients completed treatment and 425DR-TB cases were identified. The PPIA intervention increases the notification of TB cases by almost 90%.

Conclusions and key recommendations: To conclude, many instances have proven that collaboration with multi-sectoral partners resulted into more case detection and effective diagnosis of TB by using the ICT. Key recommendation includes but no to limited; partnership and engagement with PPIA in other places, enhancement/ expansion of technology and community participation.

OA-331-27 Innovative interventions to enhance access to TB services for vulnerable and marginalised populations: experience from India

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Background and challenges to implementation: Universal access to tuberculosis (TB) services is critical for timely diagnosis and treatment. Low awareness about TB and poor access to health services result in delayed diagnosis, with resultant morbidity and mortality.

Intervention: Project Axshya, supported by the Global Fund, and implemented by The International Union Against Tuberculosis and Lung Disease (The Union), works through a network of nearly 1200 community-based organisations and 20 000 volunteers in 300 districts across India. It enhances the access of vulnerable and marginalized populations to TB services through two major interventions. 1) enhanced active case-finding called Axshya SAMVAD (Sensitization and Advocacy in Marginalised and Vulnerable Areas of the District), under which trained community volunteers conduct house-to-house visits creating awareness about TB and identifying those with symptoms suggestive of TB; these persons are then linked with diagnostic facilities through referral or sputum collection and transportation. 2) Unqualified rural health-care providers (RHCPs), the first point of contact for the majority of rural and urban poor, are trained to identify those with symptoms of TB and refer them immediately for sputum examination to the nearest public health facility. They also provide directly observed treatment, short-course (DOTS), for which they get incentives. We report the results of a project to enhance access to TB services.

Results and lessons learnt: From April 2013 to December 2015, 8.9 million households comprising over 35 million vulnerable and marginalised people were visited. Out of 589 156 TB symptomatics identified, 306 192 (52%) were tested at the nearest diagnostic facility, including sputum collection and transportation for 244 847 (80%). 22 901 (7%) patients were diagnosed with TB and 22 176 (97%) were successfully initiated on DOTS treatment. The project also trained 25 331 RHCPs who referred 146 493 TB symptomatics, of whom 96 994 (66%) were tested, and 11 798 (12%) were diagnosed with TB and initiated on treatment.

Conclusion and key recommendations: Enhanced active case-finding and engagement of RHCPs through community-based organisations successfully enhances access to diagnosis and treatment of TB for vulnerable and marginalised populations. This model can be replicated in other high TB burden countries.

05. Improving patient care in MDR-TB

OA-332-27 Examining the fall-out points in the pathway to MDR-TB treatment: a gap study in Lesotho

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Background: Access to MDR-TB treatment is impeded by a complex diagnosis with high lost to follow-up (LTFU) rates, yet few studies have researched and quantified MDR-TB pre-treatment loss. This study spotlights parts of the pre-treatment MDR-TB pathway where and why the greatest challenges are encountered in Lesotho. The objective was to inform policies and interventions to curb patient loss along the cascade.

Methods: The authors mapped the complex patient pathway to MDR-TB treatment initiation and gathered data at each step to measure LTFU rates in a retrospective, descriptive study with quantitative and qualitative components. Three districts were sampled based on TB notification rates, comprising of hospitals, clinics and health centres ($n = 14$). Data was gathered from patient and laboratory registers, and national laboratory and MDR-TB initiation databases between 2013 and 2014. Questionnaires were administered to lab technicians, sample transporters, health facility and hospital staff, TB officers and patients ($n = 16$). Data was cleaned and analysed using Stata v.13 and Microsoft Excel.

Results: The majority of losses occur at the start of the cascade at case identification. Only 11% of the 203 presumptive DR-TB cases registered for first-line TB treatment underwent DR-TB testing. Nationally, only 47% of the 8.7% of the unique samples testing MDR-TB positive or Rif-resistant, were initiated onto MDR-TB treatment. In the study districts, approximately 84% of MDR-TB positive cases were initiated onto treatment. Delays were longest for LPA and culture tests with time to results at 79 days and 88 days respectively. Time to initiation from results for LPA and culture was 142 days and 175 days respectively. These results corroborate with reported challenges regarding long turnaround times from health staff and difficulties and delays in linking patients to MDR-TB treatment.

Conclusions: By understanding and addressing the largest gaps in the MDR pathway, more patients can be identified earlier, and initiated onto treatment. Some key recommendations include to: streamline patient registers to increase case identification and presumptive DR-TB testing referrals, decrease laboratory delays by optimizing processes for LPA and culture, decrease turnaround time to facilities through improved communication methods and improve linkages to care from testing to MDR-TB treatment initiation.

OA-333-27 An innovative approach for designing and implementing drug-resistant tuberculosis treatment adherence interventions

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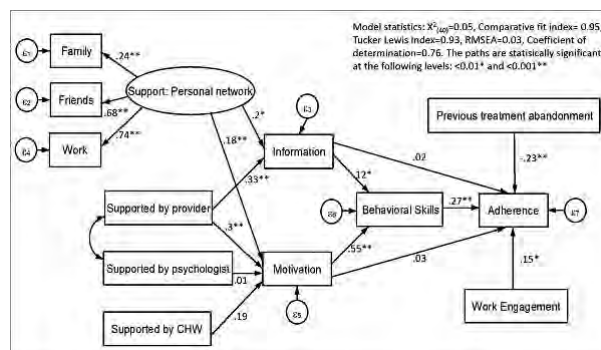
Background: Drug-resistant tuberculosis (DR-TB) continues to spread at an alarming rate. Available treatments are expensive, long-lasting, and can cause severe side effects. Diagnosed patients also face socio-economic, psychosocial, and systemic barriers to treatment adherence. In Lima, Peru, DR-TB treatment abandonment rates reached over 30% in 2015. This study aimed to estimate and model the effects of the key determinants of treatment adherence in order to guide intervention design and implementation.

Methods: We used a structured questionnaire to collect data from 326 adults diagnosed with DR-TB and 86 of their healthcare providers from 40 health centers in Lima, Peru. The main outcomes and measures were adherence rate (during the two months prior to data collection); adherence information, motivation, and behavioral skills; previous treatment abandonment; providers' work engagement; and patient-perceived psychosocial support from their social network. The model includes two validated scales: the Information-Motivation-Behavioral Skills scale and the 17-item Utrecht Work Engagement scale.

Results: Structural equations modeling revealed that adherence information and motivation have a positive effect on adherence rate ($\beta = 0.12$, $P < 0.01$ and $\beta = 0.55$, $P < 0.001$, respectively), but only through behavioral skills; behavioral skills had a direct and positive effect on adherence rate ($\beta = 0.27$, $P < 0.001$). The number of abandoned episodes had a direct negative effect ($\beta = -0.23$, $P < 0.001$), whereas providers' work engagement had a direct positive effect ($\beta = 0.15$, $P < 0.01$) on adherence rate. Psychosocial support from patients' personal social network (family, friends, work), and providers had indirect positive effects on adherence rate. The model explained 76% of the variance in treatment adherence rate.

Conclusions: Treatment adherence barriers can be overcome with appropriate psychosocial support. Interventions targeting adherence should be designed with adherence information, motivation, and behavioral skills as essential components, and should be delivered by healthcare providers or trained community members who interact with patients on a daily-basis.

Figure Model 1



OA-334-27 Impact of Xpert® MTB/RIF testing on treatment delays among persons diagnosed with drug-resistant TB in Johannesburg, South Africa

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Background: In 2011, South Africa improved its ability to test for drug-resistant TB (DR-TB) by introducing GeneXpert, a molecular test used to diagnose both TB and rifampicin resistance. While a reduction in time to diagnosis has been reported with Xpert, there is less evidence of reduction to time to treatment initiation (TTI). We estimated the proportion of persons diagnosed with rifampicin resistant (RR-) TB who initiated DR-TB treatment and report TTI during implementation of GeneXpert in Johannesburg, South Africa.

Methods: We retrospectively matched adult patients with laboratory-confirmed RR-TB in Johannesburg from July 2011–June 2012 (early/limited Xpert coverage) and July 2013–June 2014 (full Xpert coverage) with records of patients initiating DR-TB treatment at one of the city's four public sector DR-TB treatment sites. Patients were followed from date of sputum collection until the earliest of DR-TB treatment initiation, death, or 6 months' follow-up. We report diagnostic methods (according to the city's register), proportions initiating treatment, and median TTI.

Results: 594 were enrolled in the early Xpert cohort compared to 713 patients in the full Xpert cohort. The proportion of RR-TB confirmed cases diagnosed by Xpert increased from 43% to 61% in the early and full cohorts, respectively. In the early cohort, 362 patients (60.9%) were traced and referred to a DR-TB hospital,

and 245 (41.2%; 67.7% of those referred) initiated treatment. In the full cohort, 484 patients (67.9%) were traced and referred for treatment, and 429 (60.2%; 88.6% of those referred) initiated treatment. TTI fell from a median of 34 days (IQR 13-54) for the early cohort to 14 days (IQR 7-32) for the full cohort. In the early cohort, 6% of diagnosed cases initiated treatment within five days, as per the national target; this increased to 18.4% in 2013.

Conclusions: After the introduction of Xpert, the proportion of DR-TB patients who initiated treatment increased from 41% to 60%, and the TTI fell by 20 days, to a median of 14 days. Despite these substantial improvements, a third of patients did not initiate treatment, and only one-fifth did so within the 5-day target. Further investment in linkage to DR-TB care is needed.

OA-335-27 Improved access to MDR-TB services via decentralized service delivery model in Amhara and Oromia regions, Ethiopia

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Background: A significant gap persists in accessibility of MDR-TB services at national and regional levels. Ethiopia developed MDR-TB treatment initiating centers (TICs), created an ambulatory model, and discharged patients in TICs to the nearest health center for directly observed treatment (DOT). We present the experience of MDR-TB decentralization in two regions of Ethiopia.

Intervention: The USAID-funded Help Ethiopia Address Low Performance of TB (HEAL TB) project with the regional health bureaus has decentralized MDR-TB services since 2012. The project helped renovate and expand new MDR-TB TICs and helped expand GeneXpert sites, sputum sample referral, staff training, and mentorship. To ensure high quality services, the project supported targeted clinical mentoring, organized special clinic days, and provided continuing medical education.

Results and lessons learnt: Between January 2012 and December 2015, TICs increased from 1 to 22; annual testing for presumptive MDR-TB increased from 662 to 9597; patients ever enrolled grew from 56 in the first year to a total of 862. A total of 311 peripheral health facilities (treatment follow up centers/TFC) are providing DOT to patients who began treatment in the TICs, but were discharged after stabilization. Six-month culture negativity rate improved from 41.2% at baseline to 77.4%. The cure rate for the earlier cohort of 36 patients (October–December 2012) was 61.1% and the corresponding rate for the latest cohort of 44 patients (October–December 2013) was 70.5%. The proportion of death, failure of treatment, and loss to follow up for the latest cohort were 11.4%, 2.3%, and 2.3%, respectively. The commitment of the Ministry of Health was instrumental in the decentralization.

Conclusion: Decentralized MDR-TB services improved access and progressive improvement in quality of services and treatment outcome.

Table Decentralized MDR-TB services in Amhara and Oromia regions, Ethiopia

Description	Baseline	Current	% Increment
Number of TIC	1	22	2100%
Annual number of presumptive TB cases identified	662	9597	1349.7%
Annual number of MDR-TB cases on SLD	56	325	480.4%
MDR-TB cure rate	58.8%	70.5%	19.9%

OA-336-27 Achieving rapid scale-up of MDR-TB treatment using a decentralized, mixed model of patient care: lessons from Uganda

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Background and challenges to implementation: With an annual notification of 47 000 TB cases, Uganda is one of the 22 high burden TB countries. The estimated MDR-TB prevalence is 1.4% among the new bacteriologically confirmed TB cases and 12.1% among previously treated TB patients. Due to health system constraints, the majority of diagnosed patients could not access treatment prior to 2013.

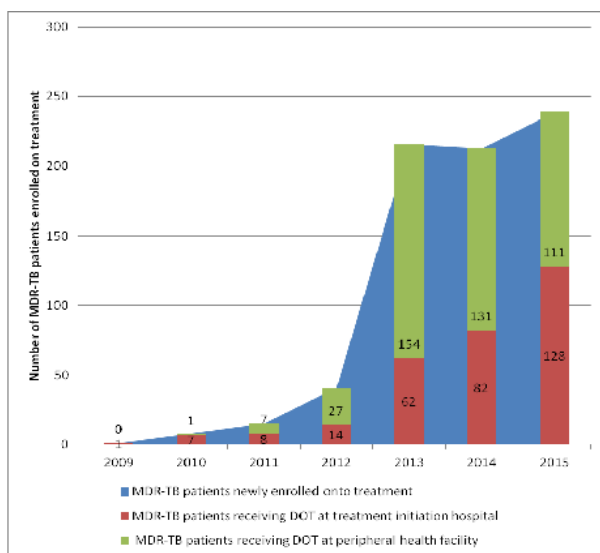
Intervention or response: The National TB and Leprosy Programme— with support from the USAID-funded TRACK TB Project, Global Fund, and other partners— decentralized treatment of MDR-TB to regional hospitals using the mixed model of care (ambulatory care and hospitalization). Multi-disciplinary MDR-TB care teams were established at each hospital through training and mentorship, provision of logistical and operational support for capacity building for peripheral DOT facilities, contact screening and investigation, and provision of patient transport. Treatment initiation and monthly clinical/laboratory evaluation occur at regional hospitals while daily DOT is provided at peripheral facilities. MDR-TB cohort review activities were conducted for programme monitoring and the MTB/RIF technology was rolled out to enhance early detection of rifampicin resistance.

Results and lessons learnt: Thirteen additional MDR-TB treatment facilities were established, a 5-fold increase in treatment access points, and an 11-fold increase in enrollment from 64 in 2012 to 732 (63% male, 3% children) by 2015. Interim and final outcomes for eligible patients indicated 78% culture conversion at 6 and 8 months, and treatment success rate of 68%, similar to hospitalization outcomes. Decentralisation of care and

patient ambulation addressed the gap in access to MDR-TB treatment.

Conclusions and key recommendations: Decentralization and use of the mixed model of patient care rapidly improves access to MDR-TB treatment with optimal outcomes. We recommend the approach for MDR-TB prevention and control in settings with similar challenges.

Figure MDR-TB patient enrollment using the mixed model of care and distribution by DOT site



OA-337-27 Management of MDR-TB: transition from hospital to community-based management in Bangladesh

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Background and challenges to implementation: Bangladesh is a high-burden TB country. MDR-TB in Bangladesh was estimated 4700 cases in 2014 with 1.4% among new and 28.5% among retreatment cases. Limited inpatient facilities and prolonged periods of hospitalization for treatment severely impedes MDR-TB management. USAID TB CARE II project introduces community based management of MDR-TB to increase access to treatment.

Intervention or response: The intervention was initially tested in 3 sites before expanding to cover 39 districts of the country by the end of the project in 2015. The key elements of the project strategy included *upazila* (sub-district) based outpatient DR-TB teams for clinical and programmatic management of patients, supervised DOT, social support to patients, and monitoring and supervision. Outpatient DR-TB teams were formed and trained in each sub-district (*upazila*). These teams are responsible for training of the DOT providers, clinical assessment of patients on treatment and monitoring and supervision.

DOT providers from health workers, living nearest to the patient, were trained to provide daily DOT, check patient's response to treatment, counsel and manage side effects, refer patients with complications to upazila doctor, and ensure follow up diagnostic needs. Monitoring and supervision is integrated with the local health system. A mobile phone based mHealth application was introduced for real time monitoring of DOT, patient's response to treatment and treatment outcomes.

Results and lessons learnt: The project strategies were successful to increase enrollment to treatment and quality of services. Rapid transfer of patients to community helped increase yearly treatment enrollment from 390 in 2011 to approximately 1000 in 2014. Treatment initiation delay after diagnosis reduced from >2 months to <1 week. Most importantly, the patient centered care significantly improved treatment outcomes. Analysis of project data for the initial 77 patients showed a treatment completion of 84% and no report of treatment interruption.

Conclusions and key recommendations: The community based management of MDR-TB showed a great potential for Bangladesh to increase access to and quality of MDR-TB services. The results suggests that a high cure rate with minimal treatment interruption and failure is achievable.

OA-338-27 Integration of MDR-TB contact tracing as part of DOT is efficient and cost-effective

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Background and challenges to implementation: Contact tracing of the index TB patients is a simple and effective way for the early finding of cases to reduce further transmission and initiating treatment for better outcome. While contact tracing has been used extensively as a control strategy for TB in the developed world, it is uncommon in developing countries with high prevalence. Investigating the contacts of index MDR-TB patients is utmost important to diagnose the cases early and reduce the transmission.

Intervention or response: Under the umbrella of NTP Bangladesh, TB CARE II Bangladesh has taken a special initiative of contact tracing of MDR-TB patients which is inexpensive and simple. The contact tracing has integrated with the routine administration of DOT to the MDR-TB patients. While visiting MDR-TB patients home to administer DOT, the DOT providers investigate symptomatic TB cases among the family members of the patient. Contact training has also been made a part of the routine monitoring and supervision system of the project staff. During field visits, project staff also identify the TB symptomatic contacts. All the TB symptomatic cases are referred for GeneXpert test for rapid diagnosis. The initiative formally started in February 2014 and gradually covered majority of the MDR-TB patients.

Results and lessons learnt: Data from February 2014 to June 2015 have been collected and analysed. Within the mentioned period a total 1854 index MDR-TB cases house have been screened. From these households, 825 symptomatic were found and tested by GeneXpert. Out of those symptomatic, 66 (8%) are found to be *Mycobacterium tuberculosis* positive and 18 (2%) are rifampicin resistant.

Conclusions and key recommendations: A significant number of TB and MDR-TB cases could be identified by adaptation of a simple strategy without any extra cost. Adaptation and integration of contact tracing with DOT and routine monitoring visit could help to find more MDR-TB cases early and ultimately reduce the residual transmission of MDR-TB.

OA-339-27 Burden of MDR-TB among contacts of MDR-TB cases: results from routine program implementation in two regions of Ethiopia

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Background: Investigating household contacts of MDR-TB index cases is one of the strategies recommended to improve MDR-TB case finding. We present the yield of routine household contact investigation for index MDR-TB cases newly initiated on treatment. The evaluation period covers TB contact screening results within 6 months of initiation of treatment.

Intervention: Facility level and home visit screenings were conducted, focusing on household contacts of index MDR-TB cases. The project supported training, mentorship, and distribution of Standard Operating Procedures, and provision of recording/reporting forms.

Results and lessons learnt: During October 2014–December 2015, household contacts of 272 MDR-TB index cases were screened for signs and symptoms of TB. TB screening was conducted for a total of 704 (95%) registered household contacts, of which 30 (4.26%; 95%CI 3.00–6.02) presumptive TB cases were identified. Out of 30 presumptive TB cases, 11 (36.7%) MDR-TB cases were identified. Among all contacts screened, 1.56% (95%CI 0.87–2.77) MDR-TB cases were identified, for a yield of 1563 MDR-TB cases per 100 000 MDR-TB contact population (95%CI 875–2776). There was no significant difference in yield of MDR-TB between the two regions ($P > 0.05$). In comparison, the yield of TB among contacts of drug sensitive (DS) TB during the same period was 0.93% (95%CI 0.84%–1.03%).

Conclusion: The project's past experience of contact screening for DS TB index cases was instrumental in expanding the service to MDR-TB contact screening. The yield of MDR-TB among contacts is seven times the TB case notification in the general population, and 1.7 times the yield of TB among contacts of DS TB index cases. Contact investigation for MDR-TB index cases

needs to be a standard practice in the MDR-TB case finding strategy.

Table The yield of MDR-TB contact investigation

Contacts screened	Amhara Region	Oromia Region	Total
Contacts screened for TB <i>n</i> (%) (95% CI)	321 (98.17) (96.06–99.16)	383 (92.07) (89.07–94.30)	704 (94.75) (92.91–96.14)
Contacts TB screen positive (presumptive TB), <i>n</i> (%) (95% CI)	11 (3.43) (1.92–6.03)	19 (4.96) (3.20–7.62)	30 (4.26) (3.00–6.02)
Contacts diagnosed with MDR-RR TB <i>n</i> (%) (95% CI)	4 (1.23) (0.49–3.16)	7 (1.83) (0.89–3.72)	11 (1.56) (0.87–2.77)
MDR-TB CNR/100 000 contacts (95% CI)	1246 (386–3160)	1828 (888–3724)	1563 (875–2776)

06. Internally displaced indigenous populations and health workers

OA-340-27 Comparative analysis of the predictive values of radiological changes to forecast the progression of pulmonary TB

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Background: The UK has been carrying out pre-entry tuberculosis (TB) screening for all long term migration visa applicants in 15 pilot countries since October 2005. Screening was subsequently rolled out to visa applicants in 101 high TB incidence (>40/100 000 population) countries. TB-typical radiographic changes have been shown to increase progression rates to active TB post pre-entry screening. This study was conducted to determine which radiological changes were associated with progression to active TB. This would provide important evidence so that screening can target the highest-risk groups.

Methods: Our study used a cohort of migrants from 15 high incidence countries screened for TB pre-entry by the International Organisation for Migration (IOM) between October 2005 and April 2012. Their pre-entry records were linked to the UK enhanced Tuberculosis Surveillance. All cases detected within 90 days of entry to

the UK were excluded as they were considered prevalent TB. Multivariable analyses were performed to identify radiographic abnormalities associated with incident TB. **Results:** The cohort consisted of 520 020 migrants screened for pulmonary TB with an overall progression rate of 82 per 100 000 person years. After adjusting for age and sex, radiographic changes associated with progression to pulmonary TB included infiltrates or consolidation (incidence rate ratio (IRR) 9.3; 95%CI 6.9–12.5), Hilar/Mediastinal adenopathy (IRR 5.4; 95%CI 3.2–9.2), single or multiple nodules or masses (IRR 5.3; 95%CI 3.2–8.9), interstitial fibrosis (IRR 4.6; 95%CI 2.7–7.9) and discrete fibrotic scar or linear opacities (IRR 3.0; 95%CI 2.0–4.5). 55% and 94% of those who developed pulmonary tuberculosis did so within 1 and 5 years of entry to UK, respectively.

Conclusions: We observed that chest radiographs classified as having infiltrates or consolidation and Hilar/Mediastinal adenopathy were associated with the highest risk of incident TB. This information could be used for targeted follow up of individuals at highest risk of TB in the UK. This would entail better coordination of pre-entry and post-entry screening to improve the health of migrants.

OA-341-27 Increasing childhood TB case detection through contact tracing strategy: a case study from rural Pakistan

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Background: Child contact tracing is an important element of TB control program to ensure early case detection and treatment. It has historically been neglected, however, in high burden and resource poor settings like rural Pakistan. An active pediatric case finding program being funded by TB REACH, was initiated in the last quarter of 2014 at 4 public sector medical facilities in district Jamshoro employing contact tracing strategies.

Methods: A contact evaluation protocol was used to investigate child contacts of newly registered patients. Health screeners were trained on using interactive algorithms on handheld android devices to make home visits to patients. The health workers took consent from the family, counseled the family on importance of screening for TB and performed verbal screening on all children aged 0–14 years living in the same household with the patient. Presumptive cases were referred to the health facility. The contacts that did not come to the clinic were given a home visit for verbal assessment and were reminded to come to the clinic for evaluation. To remove financial barriers families were provided with Rs500 towards their travel cost.

Results: A total of 829 families were evaluated. 611 (46%) families came directly to clinic, where 1605 children were assessed. Among the 151 (9.4%) children

diagnosed with TB through clinical contact tracing, 86 (57%) were aged <5 years with a median age of 4 (0–14) and 98 (65%) were male. 218 families (54%) came in through household visits. 1297 child contacts were screened, of whom 526 were investigated and 87 (6.7%) were diagnosed with TB. 36 (40.2%) were aged <5 years with a median age of 4 and 54 (62%) were male. The yield for clinical contact tracing was 9.4% while for household contact tracing it was 6.7%.

Conclusions: Household visits resulted in 36.6% of all cases detected through contact tracing strategy which resulted in an increased yield of 57.6%. It shows that basic interventions can go a long way in resource poor settings like rural Sindh where pediatric TB is highly under diagnosed and many health facilities don't even acknowledge childhood TB.

OA-342-27 Childhood TB management in camps and host communities for internally displaced person in Adamawa State, North-East Nigeria

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Background: More than two million persons are internally displaced to camps and host communities due to insurgency in North-East Nigeria. Fifty-six per cent are children aged 0–17 years, with 23% unaccompanied. Overcrowding and poor living conditions in IDP camps are risk factors for TB. Newborns of mothers with TB, HIV-infected and severely malnourished children are more at risk of contracting and dying from TB disease. Childhood TB is often missed or overlooked due to non-specific symptoms, and difficulties in diagnosis, and worsened by poor access to comprehensive health-care services.

Methods: With funding from PEPFAR/USAID, FHI360 in collaboration with other partners including UNICEF/EU supported 'Adamawa State Agency for Control of HIV/AIDS' to provide HIV testing services, hepatitis, TB screening and treatment services to IDPs in four official camps and host communities in Adamawa state, North-East Nigeria, between January–December, 2015. Other services provided were health education, food and nutrition assessment, counseling and supplements. Infection prevention and control measures, Water and Sanitation Hygiene (WASH) services, et cetera, were also provided. Records of children aged 0–17 years who were screened for TB, HIV and malnutrition were retrospectively analyzed.

Results: A total of 2500 children aged 0–17 years were screened for TB and HIV, of whom 4.7% (117) were presumptive cases and were referred to health facilities for diagnosis. Twenty-three (19.7%) children diagnosed with TB commenced treatment immediately while those

without active TB were placed on IPT. Five adults already diagnosed with TB and on TB treatment before the displacement were identified. Out of 207 (129 females, 78 males) IDPs who tested positive for HIV, 9% (18, 13 females, 5 males) were children aged 0–17 years. Twenty-six (13%) of these were adults already receiving HIV treatment before the displacement. The newly diagnosed HIV-positive cases (adults and children) were all linked to ART services. Of the total 209 577 children assessed for various illnesses including malnutrition, malaria, and pneumonia 6444 (3%) had severe malnutrition with vomiting and diarrhea while 25 511 (12%) had mild to moderate malnutrition..

Conclusions: Integrated Management of Childhood Illnesses (IMCI) is recommended for children in congregate settings such as IDP camps and conflict communities, as this approach will provide opportunities to increase childhood TB case detection and effective management.

OA-343-27 Improving TB case finding and treatment adherence in underdeveloped ethnic minority areas: China's experience

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Background: In China, TB prevalence and incidence were consistently higher in western remote areas with ethnic minority and poverty. To improve TB case finding and treatment adherence, we conducted a pilot study in one town selected from Yining county (33 ethnic minorities) in Xinjiang autonomous region (highest TB notification rate nationwide) in China from October 2014 to March 2015, supported by World Health Organization project and local government.

Interventions: Enhanced TB control measures were adopted based upon DOTS strategy and NTP. First, TB education was delivered in various ways. In 22 Masjids, well trained imams integrated TB knowledge into daily preaches, totally covering 20 440 person times. Pupils in 7 schools were educated and to spread TB knowledge to their relatives, covering around 7000 persons. Meanwhile, active case finding was conducted. All residents were screened for suspicious PTB symptoms and educated by village doctors. People older than 65 years were provided with free chest radiographic examination. Those who had abnormal symptoms or chest radiographic results were referred to TB designated hospital for further examination. Transportation and living subsidies were provided to TB patients during treatment courses.

Results and lessons learned: The number of people visiting doctors for TB increased by 104% compared with the corresponding period the last year. Among them, 55% visits were attributed to the new educational

interventions. For people <65 years old, six patients were diagnosed through active symptom screening, accounting for 7% of people with abnormal symptoms and 49/100 000 in prevalence. Ten patients were diagnosed through elderly screening, accounting for 2% with abnormal results and 1445/100 000 in prevalence. The total number of patients notified comparatively increased by 85%. The adherence rate, evaluated by timely drug collection and at least two times sputum examination, was 95% among patients with subsidy motivation, higher than no subsidy cases (49%). The positive impacts of interventions were widely accepted by interviewed healthcare workers, while heavy workload and limited human resource in active screening were mainly concerned.

Conclusions: The case finding and treatment adherence in underdeveloped minority area had been improved by integrated TB control measures. Further research is needed to explore the cost-effectiveness and sustainability.

OA-344-27 Factors associated with active TB in an indigenous population in Brazil: a case-control study

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Introduction: Although tuberculosis (TB) remains is a main public health problem in Brazil, its distribution is not homogeneous. There is highest concentration of cases in the poorest regions and in some vulnerable groups of population. In the central-west region, in particular, the incidence rates are around four times higher, comparing indigenous and non-Indigenous groups.

Objectives: To identify factors associated with active TB in an indigenous population in Brazil.

Methods: We conducted a case-control study, which took place from March 2011 to December 2012. TB cases were identified in four municipalities, which have the highest incidences of TB, in the central-west region of Brazil. For each case of TB identified we selected two controls matched by age group and local of residence. Through standardized questionnaire were collected clinical, epidemiological and sociodemographic data. The alcohol use disorders identification test (AUDIT) was also used. Interviews were performed in a period shorter than 30 days after the start of TB treatment.

Results: The sample was composed by 168 cases and 337 controls. Active TB was associated to alcohol abuse (OR = 7.85, $P < 0.001$), in subjects who have only one room to sleep in the dwelling (OR = 2.49; $P < 0.001$), sex male (OR = 1.93; $P = 0.004$) and history of contact with other TB patients (OR = 1.71; $P = 0.029$). Also, having satellite dish at home (OR = 0.21; $P = 0.016$), as a proxy of better socioeconomic situation, and to have a scar of the BCG vaccine (OR = 0.46; $P = 0.005$) proved to be a protective factor.

Discussion: Our findings revealed that factors associated with TB among an indigenous population from central-west region of Brazil are similar to observed in other groups, especially those related to poverty, alcohol abuse and close contact with TB patients. In order to face the problem, we suggest that health authorities should prioritize the detection and early treatment of cases in the villages and invest in social and development policies.

OA-345-27 Improved tuberculosis case detection in Afghanistan: an evaluation of passive and active approaches

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Background: In Afghanistan, improving TB case detection remains a major challenge. In 2014, only half of the estimated incident TB cases were notified and notifications have decreased since peaking in 2007. Active case finding (ACF) has been increasingly considered as a way to improve TB case notifications. While access to health services has improved in the country, it remains poor and many people may go without proper care.

Intervention: From October 2011 until December 2012 we conducted three separate ACF approaches in six provinces of Afghanistan and measured the impact on TB case notification. Systematic screening for cough among attendees at 47 health facilities, active household contact investigation of sputum smear-positive (SS+) index TB patients, and screening at 15 camps for internally displaced people (IDP) were conducted. We collected both project intervention yield and official quarterly notification data. Additional TB notifications were calculated by comparing the number of cases notified during the intervention period with those notified prior to the intervention, and adjusted for secular trend in notifications.

Results: We screened 2 022 127 people for TB symptoms during the intervention, tested 59 838 with smear microscopy and detected 5046 people with smear-positive TB. The majority of cases (81.7%, 4125) were identified in health facilities but almost one-fifth were found through ACF. A 56% increase in smear positive TB notifications was observed between the baseline and intervention periods among the 47 health facilities.

Conclusion: While the majority of people with TB are likely to be identified through screening at health facilities, there are many people who may remain without a proper diagnosis if outreach efforts are not made. This is especially true in places like Afghanistan where access to general services is poor. Targeted ACF can improve the number of people who are detected and treated for TB and push towards the targets of the Stop TB Global Plan and End TB Strategy.

OA-346-27 The implications of gender on the uptake of isoniazid preventive therapy in Zulu communities of uMgungundlovu District, South Africa

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Background: In a mixed methods study of isoniazid preventive therapy (IPT) effectiveness amongst Zulu communities in uMgungundlovu District, we found that community-level challenges to IPT completion included clinic utilisation and fear of reprimand among those who stopped taking therapy. Furthermore, women were much more likely to initiate IPT compared to men ($P < 0.0001$). As such we examined gender roles and health implications to develop recommendations for improving future preventive efforts.

Methods: To learn about local perspectives on IPT-use, we interacted regularly with three communities in uMgungundlovu between 2011–2015. Data collection included ethnographic observation at clinics, public meetings, and community ceremonies and regular contact with key informants. In 2014–2015, we facilitated eight focus group discussions with community members and undertook nine interviews with people who were offered IPT. Transcripts and field notes were coded in NVivo 10.0 and analysed using qualitative content analysis. Findings were member checked and discussed with community advisory teams for validity.

Results: Women were often characterised as obedient and trusting caregivers while men were portrayed as strong and sceptical providers. These gender expectations appeared to encourage silence and shame and perpetuate a cycle of lateral violence within the community. While male roles were better respected, men were often shamed by both sexes for their silence and lack of participation in health seeking and caregiving. Conversely women were often compelled to silence for fear of appearing disobedient in healthcare and other community interactions. Despite this social pressure, some women who we identified as resilient were sought as patient advocates by community members, although still faced stigma and shame. Assets within these communities currently exist to counter these potentially dated gender stereotypes.

Conclusions: Gender roles within these communities can feed a cycle of lateral violence that may prevent some men from seeking care at clinics and women from reporting health complications, both of which may affect TB preventive therapy and other healthcare initiatives. To address these challenges, we suggest community-based activities that identify systemic issues feeding lateral violence and foster strengths such as resilience and caregiving regardless of sex. We are currently working with communities in this regard.

OA-347-27 Influence of quality of work life on motivation and retention of local government tuberculosis control programme supervisors in southeast Nigeria

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Background: Retaining motivated local government tuberculosis (TB) supervisors is crucial to achieving and sustaining national tuberculosis control targets but may depend on TB supervisors' experiences and perception of quality of worklife. Nevertheless, relatively little evidence about link between quality of worklife, motivation and retention of health workers exists in Nigeria. This paper provides new evidence on influence of quality of worklife in motivating and retaining local government tuberculosis supervisors that can be used to improve tuberculosis programme performance in Nigeria.

Methods: The study took place in 5 states of southeast Nigeria comprising 95 local government areas (districts). A validated, self-administered questionnaire was used to collect data on quality of worklife (QWL), motivation and turnover intention from all local government tuberculosis supervisors in the region. Mean scores of QWL, motivation and turnover intention were calculated. Pearson correlation was used to test association between QWL, its dimensions, motivation and retention. Linear regression was used to establish relationship between supervisors' quality of worklife, motivation and supervisors' intention to leave the programme. The level of significance was set at $P < 0.05$.

Results: The mean level of QWL, motivation and turnover intention were 5.11 (0.84), 5.92 (1.05) and 2.68 (1.59) respectively. Level of education significantly predicted QWL ($\beta = -0.26$, $P < 0.05$, $R^2 = 0.06$). QWL predicted supervisors' motivation ($\beta = 0.39$, $P < 0.05$, $R^2 = 0.15$) and turnover intention ($\beta = -0.224$, $P < 0.05$, $R^2 = 0.04$). Work design explained motivation ($\beta = 0.54$, $P < 0.05$, $R^2 = 0.32$). Motivation of TB supervisors significantly influenced their turnover intention ($\beta = -0.51$, $P < 0.05$, $R^2 = 0.25$).

Conclusions: High QWL results in high motivation and low turnover intention among LG TB supervisors. Changes in QWL particularly work design are needed to motivate and retain local government TB supervisors in southeast Nigeria.

07. TB mortality

OA-348-27 Negative tuberculin skin test result in patients with active TB is associated with increased mortality risk during TB treatment

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Background: The tuberculin skin test (TST) is a widely utilized method to determine if a person is infected by *Mycobacterium tuberculosis*. However, an estimated 30% of patients with culture-positive TB disease have a negative TST. Previous studies found a negative TST increased the risk of death among persons with active TB disease but the contribution of underlying immunosuppression to this risk is unknown. We aimed to determine if a negative TST increased the risk of mortality during TB treatment after adjusting for immunosuppressive conditions.

Methods: We conducted a retrospective cohort study among culture-positive TB cases aged >15 years reported to the Georgia State Notifiable Disease Surveillance System from 2009–2014. Induration size was classified based on US Centers for Disease Control's guidelines and considered positive if a) >5 mm for persons with HIV, b) >10 mm for persons with low to medium TB risk factors, and c) >15 mm for persons with no known TB risk factors. Immunosuppressive conditions were collected from the surveillance data and included HIV, diabetes, and end stage renal disease (ESRD). Our primary outcome was all-cause mortality during TB treatment. Log binomial regression was used to estimate risk ratios (RR) and 95% confidence intervals (CI).

Results: Among 1159 culture-confirmed TB cases during 2009–2014, 21.3% were TST negative, 46.9% were TST positive, and 31.8% did not have TST result documented. Patients with HIV (27.2%), diabetes (26.7%), or ESRD (22.2%) were more likely to have a negative TST compared to those without any of these immunosuppressive conditions (18.6%) ($P < 0.01$). Among patients with documented TB outcomes ($n = 1011$), 8.6% died during treatment. The risk of death was greater among those with a negative TST (11.3%) compared to a positive TST (3.7%, RR 3.0 95%CI 1.7–5.6). After adjusting for HIV, diabetes, ESRD, age, sex and birthplace, the risk of death among patients with a negative TST was 2.6 times the risk among those with a positive TST (95%CI 1.46–5.0).

Conclusions: We found that nearly one-fourth of culture-confirmed TB patients had a negative TST at baseline. A negative TST was associated with twice the risk of

mortality during TB treatment after adjusting for immunosuppressive conditions.

OA-349-27 Interferon-gamma release assay is associated with disease site and death in active TB

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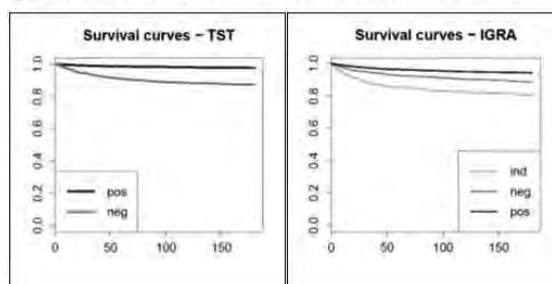
Background: While the interferon gamma release assays (IGRAs) and tuberculin skin test (TST) are primarily used to diagnose latent tuberculosis (TB) infection and aid in the diagnosis of active TB, we previously demonstrated that a negative TST in active TB disease is associated with disseminated disease and death. We sought to determine whether the same associations are present for IGRAs.

Methods: We analyzed IGRA and TST results for all persons with culture-confirmed TB disease reported to the US National Tuberculosis Surveillance System from 2010–2014. We used multinomial and multivariate logistic regression to calculate the association between IGRA and TST results and disease site and death, and constructed Kaplan-Meier survival curves by test result.

Results: 24 803 persons with culture-confirmed TB disease had either an IGRA or TST result. While persons with a positive TST had lower odds of disseminated disease (aOR 0.33 (95%CI 0.28–0.39) for miliary, aOR 0.59 (95%CI 0.51–0.67) for combined pulmonary/extrapulmonary disease), there was no difference in the odds of disseminated disease for persons with a positive IGRA. However, persons with a positive TST or IGRA had improved survival compared to those with a negative test (Figure). An indeterminate IGRA was associated with greater odds of disseminated disease and death than was a negative IGRA.

Conclusions: A positive TST, but not a positive IGRA, was significantly associated with TB disease site. Both a positive TST and a positive IGRA were associated with decreased odds of death. An indeterminate IGRA in active TB disease is not an unimportant result and is associated with greater risk of disseminated disease and death. Although the TST and IGRA are often used interchangeably, they are not equivalent in their associations with TB disease. Further study of these associations may improve our understanding of disease localization and TB-related death.

Figure 1. Survival curves for all patients with an available TST or IGRA result who initiated TB treatment.



OA-350-27 Predictors of mortality among patients registered for TB treatment in Kampala City, Uganda

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Background: According to quarterly TB surveillance data, Kampala city has a mortality above 10%, which is higher than that expected by the World Health Organization of about <5%. The cause of this high mortality is not well understood, therefore we sought to examine factors associated with it.

Methods: We conducted a retrospective cohort review of 7891 patients who started treatment during 2014 to establish and the factors that could be associated with mortality. We conducted a mortality-based analysis with sex, age, type of health facility, HIV status, disease classifications, no directly-observed-therapy (DOT) and no antiretroviral therapy (ART) at 95% Confidence Interval.

Results: Of the patients included, 61% (4795) were males, mean age was 32 (SD 13.6) and 10% (848) died. 4742 (60%) of the patients were pulmonary-bacteriologically confirmed (P-BC) and 3149 (40%) were other cases. 6196 (79%) were aged ≥40 years and 3976 (50%) of all the patients were HIV-positive. The odds of death was: among HIV-positive patients 2.8 (95%CI 2.37–3.311), among non P-BCs 2.1 (95%CI 1.860–2.49), among patients aged ≥40 years 1.54 (95%CI 1.31–1.81), no DOT 1.19 (95%CI 1.02–1.38) and no ART 1.2 (95%CI 0.93–1.57). There was no association observed between death and other factors analyzed.

Conclusions: HIV-positive status, non P-BC classification, no DOT, and age ≥40 years were independently associated with high mortality among TB patients. We recommend extra effort towards management of these categories of patients during treatment to reduce mortality of TB patients in Kampala.

Table A & B: Mortality and variables (Data source; eRegister)**Table A**

Variable	Number	Crude OR	Confidence interval	P Value
HIV+	3976	3.25	2.76 - 3.82	0.00
Age (>40)	6196	1.68	1.44 - 1.97	0.00
Not PBC	3149	2.5	2.16 - 2.20	0.00
Private Facility	2795	1.07	0.92 - 1.24	0.38

Table B

Variable	Number	Crude OR	Confidence Interval	P Value
Females	3,096	1.09	0.95 - 1.26	0.22
No DOT	3,031	1.23	1.07 - 1.43	0.004
No ART	466	1.17	0.91 - 1.51	0.22
Retreatments	635	1.14	0.89 - 1.50	0.27

OA-351-27 Exploring gender differences in treatment outcomes among TB patients in Afghanistan: a cross-sectional study

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Background: Afghanistan is a country that reported a higher proportion of tuberculosis (TB) cases among women. In 2015, 62% of reported TB cases were among women. While females comprise a higher proportion of newly reported TB cases in Afghanistan there is very little understanding of gender differences in treatment outcomes. The objective of this study was to explore TB treatment outcomes by gender.

Methodology: This was a cross-sectional survey conducted in 12 provinces using random cluster sampling of health facilities. Data from all health facilities in the cluster were collected and analyzed. The team reviewed records of study subjects (TB patients who started treatment in 2014). Researchers collected the data from TB treatment registers of health facilities in Jan 2016.

Results: Treatment records of 3221 study subjects were reviewed: 3047 (95%) patients were of category I while 128 (4%) were category II and for 46 (1%) of TB patients the treatment category was unknown. Completed data on treatment outcomes was available for 2877 (89.3%) patients: 1060 (36.8%) male and 1817 (63.2%) female and were included in the final analysis. 1652 (91%) female and 915 (86%) male TB patients successfully completed their treatment ($P < 0.01$) (Table). The death rate was 1% among for females and 3% for males ($P = 0.03$), while loss-to-follow up rates were 2% among females and 3% for males ($P = 0.05$). Transfer out rate was 5% for females and 8% for males ($P = 0.02$).

Conclusion and recommendations: Female TB patients had better treatment outcomes than males. Males were more likely to die of TB, be lost to follow up or transferred out compared to females.

Table 1: Gender distribution of TB treatment outcomes

Variable	Female	Male	P- value
Number of TB patients started treatment	2000	1185	NA
Number of TB patients evaluated for treatment outcome	1817 (91%)	1060 (89%)	$P = 0.1$
Successfully completed treatment	1652 (91%)	915 (86%)	$P < 0.01$
Treatment failure	22 (1%)	7 (1%)	NS
Death rate	24 (1%)	30 (3%)	$P = 0.003$
Loss to follow up rate	29 (2%)	27 (3%)	$P = 0.05$
Transferred out rate	90 (5%)	81 (8%)	$P = 0.002$

OA-352-27 Spatial distribution profile of mortality due to tuberculosis in an endemic city in the Brazilian Northeast

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Background: Tuberculosis (TB) is a severe public health problem in Brazil, the country ranks 16th on the list of the 22 high burden Countries. The country faces challenges concerning the international policy to end TB, with an incidence rate of 33.5/100 000 inhabitants and a mortality rate of 2.4 deaths/100 000 inhabitants. The objective was to characterize the case profile of deaths due to TB (basic cause and associated cause) and to analyze the spatial distribution of these events.

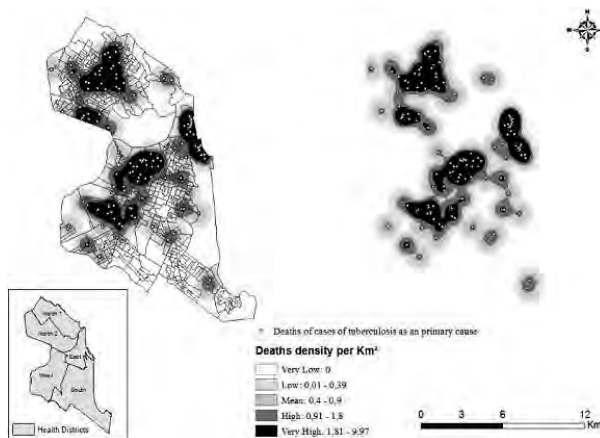
Methods: An ecological study was undertaken in the city of Natal, Rio Grande do Norte, Brazil. The population consisted of cases of deaths due to TB between 2008 and 2014, based on information from the Mortality Information System (SIM). Bivariate analysis was applied to verify the relation between the dependent variable, TB as the basic cause of death (yes or no), and the sociodemographic variables, applying the χ^2 test of proportion, with the type I error set at 5% as statistically significant. Geocoding of the cases was developed in the software Terraview and the Kernel technique was applied with a radius of 1000 meters to verify the areas with the highest density of mortality.

Results: In total, 236 deaths were identified, 154 with TB as the basic cause and 82 as the associated cause. The minimum age of the cases was 8 years and the maximum 101 years, with a mean age of 52 years. The highest death percentage was found for the male sex (72.5%), mulatto ethnic origin (53.0%), marital status single (53.0%), place of death hospital (86.0%) and not submitted to necropsy (52.5%). In the bivariate analysis, the variables age ($P = 0.001$) and education ($P = 0.008$) showed a statistically significant association with the cause of death. The thematic maps by point density demonstrated heterogeneity in the spatial distribution of the deaths,

with clustering in the areas related to the west, north and east districts (Figure).

Conclusions: the study highlights sociodemographic and operational characteristics of the death and identifies the areas most vulnerable to death by TB, which the management of health services should consider as priorities for disease surveillance actions.

Figure Maps of density of deaths due to TB



OA-353-27 Challenges to accurately estimate TB mortality: deaths in notified TB cases vs. TB deaths in vital registration system in England

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Background: An accurate estimate of TB mortality is required to monitor progress in tuberculosis (TB) control. In England, the Enhanced Tuberculosis System (ETS) collects treatment outcomes, including deaths for notified TB cases. The UK Office for National Statistics (ONS) compiles mortality statistics from the vital registration system, collected from cause of death certificates. An assessment of the death data held in each system is needed to inform our understanding of TB mortality.

Methods: TB cases notified in ETS between 2005 and 2013 were matched to ONS deaths with ICD-10 codes indicating TB as the cause of death. The following groups were compared: notified cases in ETS which matched to ONS deaths, notified cases in ETS which didn't match to ONS deaths and ONS deaths which didn't match to notified cases in ETS.

Results: In England, the number and proportion of TB cases with death as an outcome decreased from 481 in 2005 (6.1%) to 345 in 2013 (4.6%). Over the same time period, there were a higher number of ONS deaths reported (2005: 654, 2013: 587). Only 49% of ETS deaths were recorded as ONS deaths; 66% of those reported as TB causing or contributing to death and 38%

of those reported as TB being incidental to death in ETS were matched to ONS deaths. 49% of ONS deaths were matched to ETS deaths; however 7.8% of these had been denotified in ETS, mainly due to having atypical mycobacteria. 33% of ETS TB cases matched to ONS deaths did not have death as the outcome reported in ETS, with 11% having completed treatment. ONS deaths which did not match to ETS deaths were older and more likely to be born in the UK.

Conclusions: Data on TB deaths captured in the national TB surveillance system and the ONS vital registration system differ significantly. This analysis shows that further work to assess the reliability and accuracy of TB deaths reported in the vital registration system is required. A significant proportion of deaths may not be due to active MTBC, and many TB deaths reported in ETS were not captured by the ONS.

OA-354-27 Influenza pandemics and TB mortality in the 19th and 20th century in Switzerland

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Background: Tuberculosis (TB) mortality has been steadily declining in the northern hemisphere over the last 200 years, but peaked during the influenza pandemics in 1889 and 1918. We aimed to estimate the impact of the two influenza pandemics on TB mortality in Switzerland.

Methods: We analysed cause-specific monthly mortality and population counts retrieved from mortality registers and statistical reports from 1885–1900 and 1910–1925 for the city of Bern and Switzerland. We used flexible Poisson regression models with logarithmic link function to quantify the excess pulmonary TB (PTB) mortality attributable to influenza during both pandemics, and excess cancer mortality as a negative control. We restricted the excess mortality analysis to the time period from January 1, 1889 to December 31, 1894 ('Russian' pandemic), and from January 1, 1918 to December 31, 1920 ('Spanish' pandemic).

Results: Yearly PTB mortality rates increased during the influenza pandemic in the city of Bern from 370 in 1888 to 474 per 100 000 population in 1890, and from 175 in 1917 to 235 in 1919. Influenza and PTB mortality rates peaked during the winter and early spring. For an increase of 100 influenza cases (per 100 000 population), the monthly PTB mortality rate increased by a factor of 1.5 (95%CI 1.4–1.6, $P < 0.0001$) in Bern during the Russian, and by a factor of 3.55 (95%CI 0.7–18.0, $P = 0.13$) during the Spanish pandemic. For Switzerland, the excess PTB mortality attributed to influenza was also significantly increased during the Russian (2.0, 95%CI 1.8–2.2, $P < 0.0001$) and the Spanish pandemic (1.5, 95%CI 1.1–1.9, $P = 0.004$). The excess PTB mortality factor was not significantly different between the city of

Bern and Switzerland (P from test for interaction: Russian: $P = 0.45$, Spanish: $P = 0.79$), but significantly higher during the Spanish compared to the Russian pandemic (Bern/Switzerland: $P < 0.0001$). We did not observe any excess cancer mortality during the influenza pandemics.

Conclusions: We showed an excess TB mortality during the influenza pandemics in the 19th and 20th century in Switzerland. This historic analysis supports recommendations for influenza vaccination in TB patients.

OA-355-27 Associations of influenza vaccination with incident tuberculosis and all-cause mortality among elderly Taiwanese patients

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Background: Influenza vaccination is a safe and effective method for preventing infections among elderly people. Animal studies have also demonstrated that influenza vaccination may protect against tuberculosis (TB) through a Th17 response. However, little is known regarding the association between influenza vaccination and subsequent TB development. This nationwide population-based cohort study aimed to evaluate the association of influenza vaccination with incident TB and all-cause mortality among elderly Taiwanese patients.

Methods: This study included patients who were ≥ 65 years old between January 1, 2005 and December 31, 2005, using the Taiwan National Health Insurance Research Database. Data regarding annual influenza vaccinations were extracted for all included patients and time-dependent Cox proportional regression analysis was used to evaluate the associations of influenza vaccination with incident TB and all-cause mortality.

Results: Among the 99 982 elderly patients (64 290 vaccinated and 35 692 unvaccinated patients), 1141 (1.14%) and 35 234 (35.2%) patients had incident TB and all-cause mortality, respectively, during the 738 367 person-years of follow-up. The cumulative incidences of TB were 145.2 and 175.5 cases/100 000 person-years among vaccinated and unvaccinated elderly patients, respectively ($P = 0.002$). After adjusting for demographics and comorbidities, the time-dependent Cox proportional hazards model revealed that influenza vaccination was an independent protective factor for incident TB (adjusted hazard ratio [HR], 0.87; 95% confidence interval [CI], 0.77–0.99) and all-cause mortality (adjusted HR, 0.116; 95% CI, 0.11–0.12).

Conclusions: This study suggested that influenza vaccination was associated with a lower risk of TB incident among elderly patients. Further investigation of biological mechanisms is warranted.

08. 'The long and winding road': latent TB infection testing and treatment

OA-356-27 The global burden of latent tuberculosis infection

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Background: The existing estimate of the global burden of latent TB infection (LTBI) as 'one third' of the world population is nearly 20 years old. Given the importance of controlling LTBI as part of the End TB Strategy and eliminating TB by 2050, and given changes in demography, scientific insights and progress in TB control, it is important to re-assess the global burden of LTBI.

Methods: We constructed trends in annual risk in infection (ARI) for countries between 1934–2014 using a combination of direct estimates of ARI from LTBI surveys, and indirect estimates of ARI from applying the revised 'Styblo rule' to World Health Organization (WHO) estimates of TB prevalence from 1990–2014. Gaussian process regression was used to generate ARIs for country-years without data and to represent uncertainty. Estimated ARI time-series were applied to the demography in each country to calculate the number and proportions of individuals infected, recently infected (infected within 2 years), and recently infected with isoniazid-resistant strains. Resulting estimates were aggregated by WHO region. We estimated the contribution of existing infections to TB incidence in 2035 and 2050.

Results: In 2014, the global burden of LTBI was 23.0% (20.4–26.4%) amounting to approximately 1.7 billion people. WHO South-East Asia, Western-Pacific and Africa regions had the highest prevalence and accounted for around 80% of those with LTBI. Prevalence of recent infection was 0.8% (0.7–0.9%) of the global population, amounting to 55.5 (48.2–63.8) million individuals currently at high risk of TB disease, of whom 8.5% (7.6–9.6%) was isoniazid-resistant. Current LTBI alone, assuming no additional infections from 2015 onwards, would be expected to generate TB incidences in the region of 14.9 per 100 000 per year in 2035 and 8.7 per 100 000 per year in 2050.

Conclusions: In 2014, the global burden of LTBI affected approximately 1.7 billion individuals, just under a quarter of the global population. Investments in new tools is urgently needed to address this latent reservoir if the 2050 target of eliminating TB is to be reached.

OA-357-27 Diagnostic accuracy of a novel C-Tb skin test for LTBI: results from two Phase III trials

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Background: Statens Serum Institut has developed a novel specific skin test, C-Tb, based on the antigens ESAT-6 and CFP10. C-Tb combines the field friendliness of the PPD Tuberculin Skin Test (TST), with the high specificity of the interferon gamma release assays (IGRA). This presentation comprise results from two recently completed Phase III trials (TESEC-05 and -06). **Materials and methods:** The TESEC-06 trial included 979 participants from 13 clinical trial sites in Catalonia, Galicia and Basque Country (Spain) with various risk of *M. tuberculosis* infection. The TESEC-05 trial included 1090 participants with symptoms of TB and 100 endemic controls both from Cape Town (South Africa). In both trials, C-Tb and TST were administered in a double-blinded fashion to one or the other forearm. Skin indurations were read 2–3 days later, a reading ≥ 5 mm was considered positive for TST and C-Tb (cut off determined in Phase II trials). Blood for IGRA testing (Quantiferon, QFT) was drawn prior to skin testing.

Results: C-Tb had comparable specificity to QFT (both 97%, 253/262), and there was no impact of BCG vaccination. In contrast, previous BCG vaccination had a strong negative impact on TST specificity, 62% (67/108) compared to 95% (99/104) in BCG unvaccinated ($P < 0.001$). Sensitivity of C-Tb and QFT was comparable in patients with confirmed TB 77% (235/307) vs. 81% (250/307) ($P = 0.08$). In contacts, there was a strong trend in increasing C-Tb test positivity with *M. tuberculosis* exposure, on-par with QFT (95%, 783/834). The impact of age and HIV infection on C-Tb reactivity was assessed in 1090 individuals with symptoms suspect of TB disease. C-Tb as well as TST and QFT reactivity was negatively impacted by age < 2 years and CD4 T cell count < 100 cell/mm³.

Conclusions: C-Tb has comparable diagnostic performance to QFT, and addresses the problem of false positive TST results in BCG vaccinated. The C-Tb test could allow for improved target treatment of *M. tuberculosis* infected in resource restraint settings.

OA-358-27 Performance of screening tests for latent tuberculosis in young, foreign-born children using latent class analysis

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Background: Young foreign-born children (< 5 years old) from TB-endemic areas are a key population to

screen for latent tuberculosis (TB) infection (LTBI) for a number of reasons. They are at relatively higher risk to progress to active TB disease than older children and adults. TB may also present with non-specific symptoms in this population, resulting in delayed diagnosis and significant morbidity. Furthermore, preventive efforts directed at young children are likely to be cost-effective because of the potential to prevent disease over a long lifespan. However, testing of foreign-born children is frequently complicated because of recent BCG vaccination, which may lead to false-positive tests.

Design/methods: The TB Epidemiologic Studies Consortium is conducting a multicenter cohort study examining the performance of the three available tests for LTBI: tuberculin skin test (TST) and two interferon gamma release assays (IGRAs)-QuantiFERON Gold in-tube (QFT) and T-SPOT.TB (TSPOT). We performed a Bayesian latent class analysis on data from the first 471 foreign-born, HIV-seronegative participants < 5 years of age. The standard U.S. cut points were used for TST interpretation, and ≥ 5 spots was counted as positive for the TSPOT.

Results: Latent class analysis estimated a LTBI prevalence of 4.4% in this cohort. The sensitivities of the TST, QFT, and TSPOT were 70.9% (95% credible interval (95CrI) 63.2–77.9%), 72.6 (95CrI 62.7–81.6%), and 63.1% (95CrI 53.3–72.4%), respectively; no significant differences in sensitivity were noted among the three tests. Conversely, the specificities of the TST, QFT, and TSPOT were 73.9% (95CrI 69.7–77.8%), 99.4% (95CrI 98.1–100%), and 99.3% (95CrI 98.2–100), respectively, and both the QFT and TSPOT were significantly more specific than TST. The positive predictive value (PPV) of the TST, QFT, and TSPOT was 11.1% (95CrI 6.2–17.0%), 83.8% (95CrI 56.4–99.3%), and 81.4% (95CrI 56.4–98.6%), respectively.

Conclusions: Using latent class analysis in this large cohort of foreign-born children under 5 years of age, the available tests were about equally sensitive for LTBI, but the greater specificity of the IGRAs was a significant advantage. Close to 90% of positive TSTs in these children were false-positive; using either a QFT or TSPOT seems a preferable screening strategy in this population.

OA-359-27 National roll-out of latent tuberculosis testing and treatment for new migrants in England: retrospective evaluation in a high TB incidence area

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Background: The Collaborative TB Strategy for England aims to significantly reduce TB in England and national implementation of new migrant latent TB infection (LTBI) screening is a fundamental component to achieve the strategy ambitions. This study describes initial outcomes of the roll-out of LTBI screening in England,

using data from a high TB incidence area in London and aims to determine factors contributing to LTBI testing and treatment uptake and interferon-gamma release assay (IGRA) test positivity.

Methods: We conducted a retrospective cohort study including patients identified from 59 GP surgeries in the London borough of Newham between August 2014–August 2015. All migrants, aged 16–35 years who were born or spent ≥ 6 months in a high incidence country ($\geq 150/100\ 000$ and sub-Saharan Africa) and entered the UK within the last 5 years were eligible for screening. We carried out multivariate logistic regression analyses to identify factors contributing to LTBI testing uptake, IGRA positivity and treatment uptake.

Results: In Newham 3968 eligible individuals were offered LTBI screening, of whom 40% had an IGRA test done. The majority of patients tested for LTBI were 26–35 years old and male, and the five most common countries of birth were India, Bangladesh, Pakistan, Nigeria and Somalia. Patients born in East and South-East Asia ($OR = 0.5$, $P = 0.04$) and sub-Saharan Africa ($OR = 0.5$, $P = 0.03$) were less likely to take up LTBI testing compared to patients from the Indian sub-continent. Patients with diabetes were more likely to take up LTBI testing ($OR = 1.8$, $P = 0.02$), while patients who smoked were less likely ($OR = 0.8$, $P = 0.01$). IGRA positivity was 25.8%. Patients in the older age group ($OR = 1.9$, $P < 0.0001$) and male ($OR = 1.3$, $P = 0.04$) were more likely to have a positive IGRA result. The majority (61.8%) of patients with a positive IGRA result were prescribed LTBI treatment by their GP.

Conclusions: Conclusions from this study allow us to better understand which demographic groups should be targeted to increase acceptability of LTBI testing and treatment in the community. These findings can be scaled up nationally to ensure that the national LTBI testing and treatment programme has a large impact on TB rates in England.

OA-360-27 Community-level challenges to tuberculosis preventive therapy provision in KwaZulu-Natal, South Africa

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Background: Tuberculosis preventive therapy is identified as a pivotal tool to achieve the 90-90-90 targets. Since 2011 isoniazid preventive therapy (IPT) has been offered widely among people living with HIV in uMgungundlovu District, South Africa. uMgungundlovu has a high incidence of HIV-related TB, and public hospitals and clinics service predominantly overcrowded, marginalised Zulu communities. As such we worked with three Zulu communities to learn more about health-related explanatory models and IPT experience to help

identify community-level challenges to IPT uptake and completion.

Methods: This study was embedded within a larger research project on the effectiveness of isoniazid. Utilising a hybrid of community-based participatory and ethnographic methods, we undertook community and clinic observation, nine individual interviews with people offered IPT, eight focus group discussions with community members, and numerous informal interviews with key stakeholders between April 2013 to June 2015. Transcripts were coded in NVivo version 10 and analysed using qualitative content analysis. Findings were member-checked and discussed with community advisory teams for validity.

Results: Participant data suggest clinic utilisation may impede IPT implementation. General mistrust in the health system exists at multiple levels and may prevent initial health interactions. Community members often associate illness with pain, which may prevent people from seeking preventive therapy. Some participants noted that over-burdened staff were less accommodating to clients seeking preventive services. With regard to completion, paper-based IPT registers were variably maintained, and some patients were unclear about treatment length. Additionally, fear of reprimand may prevent clients from reporting adverse events and cessation of treatment to health staff. For those who complete preventive regimens, cleansing practices like vomiting and enemas may reduce efficacy.

Conclusions: Although preventive therapy contributes to the arsenal against tuberculosis, there are community-level challenges that may hinder optimal usage in rural South Africa if left unaddressed. While health system challenges appear to affect aspects of IPT implementation and completion, explanatory models of illness and general mistrust may also prevent clinic-usage and IPT follow-up. Cleansing practices may affect drug-efficacy, and healthcare providers should discuss optimal timing for cleansing and potential effects on drug action with clients at IPT enrollment.

OA-361-27 A public health evaluation of contact tracing and management in Brazil

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Background: Recent projections by the World Health Organization show that contact tracing and latent

tuberculosis infection (LTBI) treatment are necessary steps to achieve tuberculosis elimination by 2050. We performed a public health evaluation of contact investigation in three high incidence cities in Brazil, where guidelines recommend testing all contacts with tuberculin skin tests (TST) and treating those with an induration ≥ 5 mm after excluding active tuberculosis (no symptoms and normal chest X-Ray). LTBI treatment is also recommended for HIV-positive patients after close contact, regardless of TST results.

Methods: We collected indicators of the contact cascade of care from 1 January to 30 June 2014, when PPD was available without supply restrictions. Data were gathered in the official registry books, pharmacies and index cases' medical records of 12 primary care clinics in Recife, Manaus and Rio de Janeiro. We also interviewed contacts, index cases, community-health agents, nurses and physicians in the same clinics, findings are detailed elsewhere.

Results: 814 contacts from 339 registered index cases were identified (mean = 2.4 contacts/index case). Out of these, 73 (8.9%) underwent TST of whom 12 (16.4%) did not have TST read and 27 (36.9% of those read, or 3.3% of all contacts) were TST positive. All 27 started treatment, of whom 17 (62.9% of those who started treatment or 2.1% of all contacts) completed treatment.

Conclusions: The main losses in contact management precede the treatment prescription and adherence steps. First, at least 4 contacts/index case are expected to be identified. Moreover, opportunities to detect LTBI were missed in over 90% of identified contacts. Indeed, estimating 4 contacts/index case, full investigation for 90% and a 40% rate of LTBI among them, 976 persons with LTBI could be treated per year. Assuming an 80% completion rate and a 10% rate of progression to disease in untreated contacts, around 80 new cases could be avoided yearly in these clinics.

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OA-362-27 Uptake and completion of isoniazid preventive therapy among household contacts of tuberculosis cases in Lima, Peru

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Background: Isoniazid preventive therapy (IPT) can avert active tuberculosis (TB) in up to 60% of persons infected. Household contacts (HHC) of TB patients are at increased risk of developing TB infection. The Peruvian national TB program recommends that if active TB is ruled out, a six-month regimen of IPT should be started in all HHC <5 years old, and to those ages 5–19 years old who have a tuberculin skin test over 10mm. We determined the proportion of HHC that were started on IPT and that completed it.

Methods: We conducted a retrospective longitudinal study in three public health facilities in South Lima. We reviewed clinical files and treatment charts of all TB patients registered from January 2014 to June 2015 (index cases). We enumerated the HHC reported and registered their age, sex, kinship to the index case, IPT prescription, IPT start, weekly pick-up of IPT and completion.

Results: One hundred forty one index cases were registered and 501 HHCs were reported. Median age of HHCs was 24 years old (interquartile range (IQR), 10–41) and 261/487 (53.6%) were female. Sixty five (12.9%) HHCs were < 5 years old and 129 (25.7%) were ages 5–19 years old. IPT was started in 43/65 (66%) children < 5 and in 44/129 (34.1%) of 5–19 years old group ($P < 0.001$). The median number of weeks that were completed by the <5 years group was 15.5 (IQR, 9.5–24), while for the 5–19 years group it was 14.5 (IQR, 8.75–24). IPT was completed by 13/43 (30%) < 5 and by 19/44 (43%) of the 5–19 years group ($P = 0.2$). Two out of the 32 completing IPT, missed a weekly pick-up. No differences were found in HHCs completing IPT in function of their kinship to the index case, while HHCs < 1 year old were less likely to complete IPT than older ones.

Conclusions: In our setting, IPT uptake among eligible HHCs was moderate and completion was low. The Peruvian TB program should study the reasons for limited uptake and low completion to implement interventions to increase both.

OA-363-27 Is isoniazid preventive therapy more effective in high-burden settings? Modelling the effect of TB incidence on IPT impact

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Background: Isoniazid preventive therapy (IPT) is an effective tool for preventing active tuberculosis (TB) at the individual level, although understanding of its mechanism of action is poor. As its ability to reduce TB incidence in high burden settings may be limited, the World Health Organization recently recommended targeting this intervention to low incidence settings. However, the optimal disease burden for IPT use has not been defined. In this study, we describe for the first time the relationship between TB burden and the anticipated effect of IPT and we determine the optimal incidence for IPT implementation.

Methods: We constructed a model of TB transmission dynamics to investigate IPT effectiveness under various

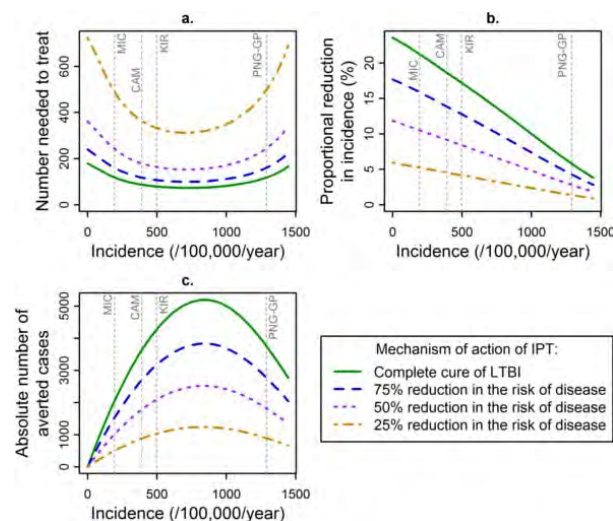
epidemiological settings. The model structure was intended to be highly adaptable to uncertainty in both input parameters and the mechanism of action of IPT. To determine the optimal setting for IPT use, we identified the lowest number needed to treat (NNT) with IPT to prevent one case of active TB.

Results: We find that the NNT as a function of TB incidence shows a 'U-shape', whereby IPT impact is greatest at an intermediate incidence and is attenuated in both lower and higher incidence levels. This U-shape was observed over a broad range of parameter values, and the optimal TB incidence was generally greater than 500 cases/100 000/year. This finding remained valid under any assumption regarding the individual effect of IPT.

Indicative levels of TB incidence represented for Indonesia (IDN), Cambodia (CAM), Kiribati (KIR) and the Gulf Province of Papua New Guinea (PNG-GP).

Conclusions: TB burden is a critical factor to consider when making decisions about IPT community-wide implementation. We demonstrate that the optimal incidence for applying this intervention is likely to be higher than previously thought; a finding with substantial implications for global TB-control policies.

Figure Variation of IPT impact over TB incidence



09. The changing landscape of tobacco control

OA-364-27 Child labor in bidi factories: current situation and way forward

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Background and challenges to implementation: *Bidi* is one of the major tobacco products consumed in Bangladesh with about 65 000 people direct employed

in 117 bidi factories in the country. Along with their some associate labor, a significant proportion of these workers is children. In this context, it is important to explore the child labor situation in bidi factories to highlight the need for regulating this harmful sector in light of the prevailing laws and policies of the country. The study was conducted in four regions of Bangladesh with the highest concentration of bidi factories: the districts of Rangpur, Kushtia, Tangail and Barisal. A total of 160 child laborers (ages 7–14 years) and 160 parents were interviewed by a semi-structured questionnaire. For the qualitative section, 28 in-depth interviews were conducted among experienced workers, factory management and doctors.

Intervention or response: Survey findings revealed that most of the children were from poor families with an income of less than 5000 Taka (US \$63) per month. About half of the respondents' children were working in the factories for 2–4 years. The number of working days for the children varied across regions: 4/10 children worked over 6 hours a day and 8/10 children worked over three hours a day. A quarter of the working children had dropped out of school.

Results and lessons learnt: The low wage rate was one of the important reasons that make bidi factory owners interested in employing child laborers. The survey revealed that more than 8 of 10 child workers felt sick (headache & breathing problems) during their work.

Conclusions and key recommendations: Enforcement of a strong policy with legislative bindings is necessary. Government support in the form of safety-net programs can be introduced. Finally, people, particularly the parents, need to be aware of the adverse effects of working in bidi factories. Government, media and NGO-CSOs should work collectively to stop child labor in bidi factories.

OA-365-27 Who is accountable for tobacco control in India? Critical analysis of stakeholders

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Background: Health Ministry in India is the nodal agency for tobacco control on the analogy of WHO under United Nations. India an obligatory to implement MPOWER under FCTC has multiple challenges including high prevalence of tobacco use and variety of tobacco products. Indian Tobacco Control Law and National Tobacco Control Program are partially covering PWE but not the MOR components of the MPOWER package. These policies involve multiple stakeholders and all MPOWER tools are not within the preview of Health Ministry.

Design and methods: A stakeholder's analysis framework by IPA has been used to generate knowledge about the relevant actors, their interests and scope for implementation the MPOWER in India. The main stakeholders are Health Ministry, NGOs, researchers, media, police,

judiciary, trade and Commerce Ministry, Information and Broadcasting Ministry, Finance Ministry and Agriculture Ministry.

Results: Health Ministry has adequate scope for Monitoring tobacco (M) and Offering help to quit (O) but limitations as law enforcer to Protect people (P), ensuring pack Warnings (W), TAPS ban (E) and Raising tobacco taxes (R). NGOs and researchers are the key for policy advocacy and analysis. Media is neutral. Police not being the primary stakeholders are contributing for law enforcement. Judiciary support is outstanding. Ensuring pack warnings (W) and regulating tobacco advertisements (E) are within the preview of Trade/Commerce and Information/Broadcasting Ministry respectively. Tobacco taxes (R) is domain of Finance Ministry and Agriculture Ministry has to safe guards the interest of tobacco farmers too.

Conclusions: Implementing comprehensive MPOWER polices is beyond the scope of Health Ministry and it requires wider approaches involving multiple stakeholders. There is an urgent need for a statutory regulatory body at National level with sufficient control on all relevant stakeholders for effective tobacco control in India.

OA-366-27 What impedes tobacco control law enforcement in China?

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Background: Since January 2006, Beijing, Shanghai and 16 other cities have implemented local tobacco control laws and regulations, but enforcement has confronted many problems. Health inspectors and law enforcement officials are the principal force for tobacco control regulation enforcement, hence their knowledge and attitude toward enforcement of tobacco laws and regulations needs to be found out, to pinpoint the real problems.

Methods: Inspectors, responsible for tobacco control inspection and law enforcement from inspection bodies at city and district levels in 11 cities that have carried out tobacco control legislation, are selected for a questionnaire survey.

Results: 1) Knowledge of health inspectors and law enforcement officials on tobacco control is neither accurate nor comprehensive. Among the surveyed persons, 45.1% and 48% knew correct answers to hazardous and carcinogenic components of tobacco smoke, relationship between second-hand tobacco smoke and disease respectively. 2) Knowledge about certain clauses in local tobacco control regulations (e.g., range of smoke-free places and responsibilities of such places) is incomplete. 57.7% gave the correct answers. 3) Most inspectors (42%) are able to accurately grasp the principles and regulations of punishment for illegitimate smoking. However, among them, only 17.7% knew how to punish illegitimate smokers. 4) Inspectors and officials are stressed out by difficulties in tobacco control law enforcement inspection to government offices.

Conclusions: 1) Amend the law to totally ban smoking in indoor areas, and simplify law enforcement procedures. 2) Enhance training on knowledge related to second hand smoking as well as denormalization of smoking. 3) Enhance training to help law enforcers fully understand local regulations. 4. Boost their sense of responsibility and confidence.

OA-367-27 Using mass media to support implementation of tobacco control policy in Viet Nam

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Background: Viet Nam ratified the FCTC in 2004 and in June 2012, the National Assembly of Viet Nam passed the country's first comprehensive tobacco control legislation, framed in line with the FCTC. World Lung Foundation (WLF) worked with the Viet Nam Steering Committee on Smoking and Health (VINACOSH) to develop and implement three phases of national mass media campaigns to educate about the harms associated with tobacco smoking and SHS exposure, and to increase support for passage of the tobacco control law. Building on a further national campaign staged in line with the implementation date of the law in May 2013, a new campaign was developed in 2014 to coincide with the introduction of smoke-free regulations in public places from December 31, 2013, and the introduction of new pictorial warnings on all cigarette packs from February 2014. The adapted campaign ads included specific images from the new graphic pack warnings and information about the new smoke-free regulations. The campaign primarily comprised graphic television advertisements broadcast nationally as well as through provincial media with the support of provincial Health Information and Education Centers (HIECs).

Design/methods: A national household survey was undertaken to assess reach and impact of the campaign, replicating the sampling methodology adopted for earlier evaluation surveys.

Results: The campaign achieved high population reach (63% prompted recall), with 87% of smokers who recalled seeing the ads reporting that the ads made them feel concerned about the effects of smoking on their health and their family's health. Amongst smokers recalling the ads, 69% reported that the ads made them more likely to stop exposing others to their smoke and 79% reported the ads made them more likely to comply with smoke-free regulations. In addition, more than two-thirds of these smokers reported that the ads made them more likely to quit and reported making a quit attempt after watching the ads. Three-quarters of non-smokers

(77%) recalling the ads reported that the ads made them more likely to complain about being exposed to cigarette smoke.

Conclusions: The findings provide further support for the role of mass media campaigns in contributing to implementation of tobacco control policies.

OA-368-27 Impact of ban on smokeless tobacco products on tobacco consumption behaviour in Punjab

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Background: There are provisions under the Food Safety and Standards (FSSAI) Act of India to curb the epidemic of Smokeless (Chewable) Tobacco, which is the major cause of oral cancers in addition to other Non Communicable Diseases in India. In the year 2012, Commissioner Food and Drug Administration Punjab, India imposed a ban on smokeless tobacco (SLT) products in the entire state. Though ban has been in place for more than three years, there is a lack of evidence regarding enforcement & implementation on ground in terms of consumption behavior of smokeless tobacco users in Punjab. The objective of the present study is to assess the impact of ban on smokeless tobacco products on tobacco consumption behavior in Punjab.

Methods: The study used mix methods design wherein 450 current tobacco users from three randomly selected districts of Punjab were interviewed using a pre-structured questionnaire consisting of 50 questions (quantitative). It was supplemented with an in-depth interview of 45 tobacco users (qualitative). The respondents were enrolled from Points of Sale (PoS) in urban and rural locations.

Results: Among a total of 450 tobacco users, 170 (37.7%) were reportedly using smokeless tobacco, of which 38 (42.7%) were aware and concerned about its ill effects. Around 150 (80%) were in contemplation phase, wherein they are thinking about quitting and 38 (42.7%) were in post-contemplation phase where tried to quit at some point of time. A majority 306 (90.8%) of users had knowledge about the ban & supported the ban on Smokeless Tobacco, but here was no perceived difficulty in buying SLT from tobacco vendors.

Conclusions: Because of the awareness drive by Food and Drug Administration Punjab, India there is a considerable knowledge about the ban and harmful effects of Smokeless (Chewable) Tobacco, however it is available at most of the Points of sale. There is an urgent requirement to take punitive action under Food Safety Standards Act of India against the violators of ban on Smokeless (Chewable) Tobacco. There is also a need to upscale cessation facilities.

OA-369-27 Analyzing partnerships: drawing lessons from the multisectoral collaboration in the implementation of the FCTC in the Philippines

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Background: In 2010, the Department of Health Philippines established the National Tobacco Control Committee (NTCC) to serve as the multisectoral body that would monitor the compliance of the Philippines to the Framework Convention on Tobacco Control. Since then, it becomes a venue to strategize and develop partnerships towards concerted and synergistic actions against the use of tobacco. The partnership becomes instrumental to the passage of Sin Tax Law and the Graphic Warning Law. The aim of this study is to analyze the partnership among members of the NTCC as an input for a more coordinative movement in the implementation of 2017–2022 National Tobacco Control Strategy.

Methods: The VicHealth Partnership Tool was utilized to analyze the partnership. The tool consists of a questionnaire with 7 open-ended questions and a checklist with 7 components and 23 questions that define features of a successful partnership. There are 18 respondents that came from different members of the NTCC. Eight of which were interviewed to elucidate further their answers. The checklist was categorized into three as prescribed by the tool. Quartile analysis was conducted to rank scores per question, while standard deviations assessed consistency of the answers across respondents. Answers to the open-ended questionnaire together with the interviews were clustered to obtain the recurring themes. All the analysis formed part the narrative.

Results: The study shows that the partnerships providing a sense of solidarity and shared responsibility. There is now a venue for information sharing, where they learn from the experience of other institutions. Sharing resources and technical expertise fill in the gaps, promote synergistic actions and lessen duplication. More heads are better than one in planning strategies and implementing actions. Bureaucratic processes have also been streamlined especially among government agencies. Despite the gains, there are procedural and administrative ambiguities especially in resolving conflicts and dealing with inactivity of members. Thus, partnership guideline is crucial.

Conclusions: The NTCC has come a long way in ensuring that the FCTC is being implemented in a coordinated manner. The partnership will continue to become relevant as the Philippines embarks to the new roadmap of multisectoral tobacco control program.

OA-370-27 How many deaths can be averted by increasing the legal age at initiation to 21 years globally?

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Background: Tobacco industry uses minors and underage youth to further its trade, thereby creating a sustainable cohort of future addicts. Many cities and jurisdictions in the US and other countries are passing local legislation to reduce the numbers of those who initiate early by increasing the age of purchase and use of tobacco products. This is to assess how many future initiations can be averted if the global age of initiation is increased to 21 years (vs. 18 in most countries, and 16 in some countries).

Intervention: We use the disaggregated data of 2015 from Institute for Health Metrics and Evaluation and the World Bank on tobacco use and initiation to measure the total number of youth who initiate between 15 and 21 years.

Results: On an immediate basis we estimate that about 50% of the total number of new initiations will be averted but 50% of others who become lifelong smokers will take up the habit. Of these who initiate, we assume that an estimated 50% of them will initiate before the age of 18 years and the remaining 50% will initiate between 18 and 21 years. Based on this assumption we estimate the future of tobacco epidemic in 2025 if the age of 21 years were to be adopted globally in 2015.

Conclusion: An early estimate based on our model, we find that increasing the age to 21 years will avert more than seven million underage cigarette users from becoming lifelong smokers. Our model is under refinement and we will present our findings at The Union World Lung Conference in Liverpool. We believe that this data will be useful for advocating to increase the age of purchase and use at the country and regional level.

OA-371-27 Cost-effectiveness of a sponge campaign in Moscow

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Background: Evidence from high-income countries has shown tobacco control mass media campaigns (MMC) to be cost-effective in reducing tobacco consumption, but similar evidence from low & middle-income countries is rarely reported. An evaluation of anti-tobacco campaign entitled Sponge, which aired in Moscow in 2010, provided evidence on the cost effectiveness of MMC in developing countries.

Methods: Standard methods of cost-benefit analysis using a societal perspective were employed. Primary data for analysis was obtained from a city representative survey of 886 smokers that was designed to test the Sponge campaign impact. Based on estimated additional quit attempt among smokers generated by the Sponge

campaign compared to status quo, number of successful quitters, burden of smokeless population such as health expenditure, disabled adjusted life years (DALYs) were calculated accordingly. Considering the cost of the campaign was US\$ 200 000, the incremental cost-effectiveness ratio (ICER) was calculated with sensitivity analysis accordingly.

Results: The Sponge campaign was found to be cost-effective in Moscow: 181 763 quit attempts and 4544 successful quitters were generated in Moscow. We also predict that the campaign reduced 23 993 years of life lost (YLL) and saved more than US \$12 million medical expenditure attributed to smoking. The ICER of the campaign was US \$8.3 per DALY and US \$133 per life saved, which is significantly lower than Moscow's 2010 yearly GDP/capita of US \$6365.

Conclusions: Findings were consistent with the evidence from high-income countries and suggested that anti-tobacco MMC can be highly cost-effective and generated significant returns on investment in developing countries.

SHORT ORAL ABSTRACT SESSIONS

01. Drugs, vitamins, valves: the diversity of TB clinical trials

SOA-500-27 Can micronutrient supplementation prevent TB in vulnerable household contacts? A randomised controlled trial

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Background: Tuberculosis is associated with low concentrations of vitamin D, vitamin A and zinc. Although these micronutrients are important determinants of anti-mycobacterial immunity and have been shown to directly inhibit anti-mycobacterial growth in vitro, studies evaluating their potential to prevent tuberculosis are lacking. We therefore undertook a double-blind, randomised controlled trial of micronutrient supplementation among household contacts of patients with tuberculosis in Callao, Perú.

Methods: 1987 household contacts aged ≥ 15 years of 708 index-cases with confirmed, pulmonary tuberculosis were recruited between 2002–2006, completed a baseline questionnaire and had their height, weight, arm circumference and skin-fold thickness measured. Contacts were randomly assigned by household to blindly receive either supplementation with vitamin D 400 IU,

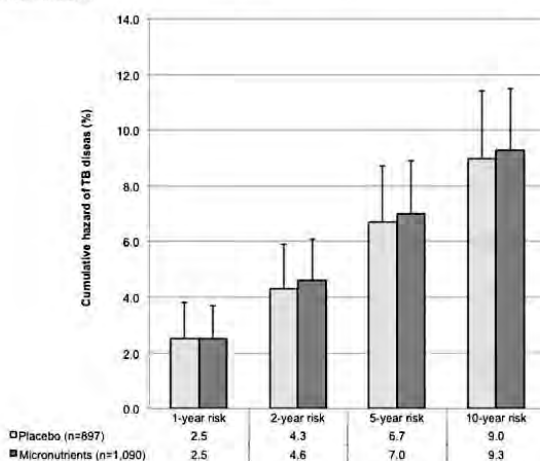
vitamin A 5000 IU and zinc 25 mg or inert placebo, once daily for six months. Contacts were visited every 2–4 weeks to ask about symptoms and perform pill counts in order to measure adherence. After six months, contacts completed a repeat anthropometrical assessment and were subsequently followed up for incident tuberculosis with collaboration from the National Tuberculosis Programme for a median 11 years. Furthermore, three prevalence surveys were performed in 2006–2007, 2012 and 2015–2016 in order to identify undetected prevalent tuberculosis.

Results: Overall, 172 contacts developed tuberculosis during 18 777 person-years (PY) follow up, equating to an incidence of 911/100 000 PY. The incidence and thus tuberculosis risk in the supplementation group: 921/100 000 PY (95%CI = 753–1126) was not significantly different to the placebo group: 898/100 000 PY (95%CI 753–1126; $P = 0.87$; Figure). There were no differences in the rates of symptoms experienced by contacts comparing the supplementation vs. placebo groups. Although all anthropometrical measurements increased at six month follow up, supplementation did not significantly affect measurements compared to placebo.

Conclusion: Six months of micronutrient supplementation provided to household contacts following tuberculosis exposure had no effect on subsequent tuberculosis disease.

Figure Risk of TB by allocation

Figure: Histograms showing cumulative hazard of TB among contacts according to assignment. Error bars represent 95% confidence intervals. The data table presents cumulative hazard at 1, 2.5 and 10 years derived from Nelson-Aalen functions.



SOA-501-27 Effect of moxifloxacin on QTc interval in adults with pulmonary tuberculosis

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Background: Moxifloxacin (MFX), a 8-methoxy-quinolone with promising anti mycobacterial activity, is being evaluated in many randomized clinical trials for shortening the duration of tuberculosis (TB) treatment. MFX

has the propensity to prolong the QTc interval in a dose-dependent manner by inhibition of potassium channels, which predisposes to ventricular tachyarrhythmia and Torsade's de pointes (TdP). Even though there is data on the cardiac toxicity of short duration MFX for acute bacterial infections there is little information on the safety of MFX when given for longer duration. We analysed the serial ECG data of the adult TB patients who were enrolled in a phase III trial to study the efficacy and safety of MFX containing regimens at National Institute for Research in Tuberculosis at Chennai, India. **Methods:** Newly diagnosed sputum positive pulmonary TB, HIV seronegative, patients were randomized to four MFX regimens of 3 or 4 months duration or a 6 month standard (control) regimen after obtaining a written informed consent. Patients in the MFX regimens received 400 mg daily MFX along with other first line anti-TB drugs. Patients with prior history of cardiac disease, an abnormal ECG or with a QTc of >450 ms at the baseline were not enrolled. ECG was recorded at baseline or pretreatment, 1, 2, 3, and 4 months post treatment. A comparison of the means of the QTc interval in the two groups was done using a *t*-test.

Results: Of the 602 patients enrolled, 476 were treated with the MFX regimens and 126 with the control regimen. The median age of the patients was 35 and 457 were males. The mean BMI was 16.3 kg/m². The mean pre-treatment QTc was 403.90 and 403.54 ms in MFX and control regimen respectively. There was no statistically significant increase in the mean QTc interval in either group of patients up to 4 months. There were no instances of arrhythmias.

Conclusions: Moxifloxacin, at a dose of 400 mg given once daily is well tolerated and without any adverse cardiac events in pulmonary TB.

SOA-502-27 Bedaquiline for extensively drug-resistant or pre-XDR *Mycobacterium tuberculosis*: interim results of an early access study

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Background: This study (TMC207TBC3001; NCT01464762) provides early access to BDQ for patients with *Mycobacterium tuberculosis* infection resistant to isoniazid, rifampin and a fluoroquinolone and/or ≥1 of the second-line injectables (SLI) amikacin, kanamycin, capreomycin (ie, pre-XDR-TB or XDR-TB) and who had limited/no treatment options.

Methods: Patients received BDQ for 24 weeks (400mg qd for 2 weeks, 200mg tiw for 22 weeks) with an

investigator-selected background regimen (BR) using ≥ 3 drugs to which the MTB isolate was likely susceptible. After completing the 24-week BDQ+BR treatment, patients received BR only for up to 96 weeks under supervision using DOTs according to NTP guidelines. Safety, tolerability and microbiological status were assessed during the study. No statistical hypotheses were tested. Results of an interim analysis after 30 (52.6%) patients completed 96 weeks are presented.

Results: 57 patients (Russia 3 sites, $n = 54$; Lithuania 1 site, $n = 3$) received BDQ+BR. All patients were white and HIV negative, 58% female, mean age 31 years; 91% had previously used second-line TB drugs. Pre-treatment, 47% had pre-XDR-TB (25% fluoroquinolone resistant; 23% SLI resistant) and 53% XDR-TB. Drugs used in the baseline BR ($>50\%$ of patients) were fluoroquinolones (100%), mainly levofloxacin (68%), PAS-C (86%), pyrazinamide (88%), capreomycin (77%), linezolid (61%), terizidone (56%). At the analysis cut-off, 31 patients had completed the study (54%), 19 were ongoing (33%) and seven discontinued (12%). Safety outcomes are summarised below (Table). In the 45 patients who had a positive baseline MTB culture and available post-baseline results, culture conversion was 69% (31/45) at 24 weeks.

Conclusions: BDQ+BR was generally well tolerated, with no new clinically relevant safety findings, and led to a good treatment outcome after 24 weeks of therapy in patients with pre-XDR-TB and XDR-TB.

Table: Safety analysis outcomes

Safety analysis during the overall treatment phase ^a	All patients (n=57)		
Total discontinuations	7 (12%)		
Discontinuations due to AEs	5 ^b (9%)		
Withdrawal of consent	2 (4%)		
Any AE (regardless of cause or severity)	50 (88%)		
Most common AEs ($\geq 15\%$)			
AST increased	27 (47%)		
ALT increased	15 (26%)		
Eosinophilia	13 ^c (23%)		
Any AE at least possibly related to BDQ	6 (11%)		
Any grade 3 or 4 AE	15 ^d (26%)		
Most common grade 3 or 4 AEs ($>5\%$)			
ALT increased (grade 3)	5 ^d (9%)		
AST increased (grade 3)	4 ^d (7%)		
Any serious AE	8 ^d (14%)		
Deaths during the study	Case 1	Case 2	Case 3
Considered related to BDQ or BR by the investigator?	No	No	No
Days since last BDQ intake	441	442	411
QTcF at Week 24 (ms)	414	436	310
Treatment phase	Post-investigational	Post-investigational	BR follow-up
TB-related?	Yes	Yes	No
	(Pulmonary hemorrhage)	(Pulmonary hemorrhage)	(Acute myocardial infarction)

^aFrom date of first BDQ intake until date of last intake of any study drug (BDQ or BR) plus 1 week; ^bIncludes 3 patients who died and two patients who discontinued BDQ due to an AE (toxic nephropathy and depression);

^cNo AEs considered at least possibly related to BDQ by the investigator

SOA-503-27 Resistance to pyrazinamide and ethambutol among MDR-TB participants in a clinical trial in Lima, Peru

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Background: Pyrazinamide and ethambutol are included in nearly all regimens for TB. Their routine administration, even to patients with risk factors for multidrug-resistant tuberculosis (MDR-TB), may contribute to widespread resistance to these drugs among MDR-TB patients. We describe the frequency of resistance to pyrazinamide and ethambutol among participants in a Phase II dose-ranging trial of levofloxacin for the treatment of fluoroquinolone-susceptible MDR-TB.

Methods: We screened 58 consenting adults with pulmonary MDR-TB or risk factors for MDR-TB from East Lima, Peru, between January 2015 and February 2016. We included 23 who had baseline isolates resistant to isoniazid and rifampin by GenoType MTB-DR^{plus} 2.0 and susceptible to fluoroquinolones by MTB-DRsl 1.0, and met other eligibility criteria for the parent study. Further drug susceptibility testing (DST) to isoniazid, streptomycin, ethambutol, pyrazinamide, and fluoroquinolones was performed in BACTEC MGIT 960. TB treatment history, prior to and during the current episode, was also recorded.

Results: Resistance to isoniazid and rifampin and susceptibility to fluoroquinolones were confirmed by DST in 100%; 18/23 (78.3%) patient isolates were also resistant to pyrazinamide and 14/23 (60.9%) to ethambutol. Prior to study enrollment but during the same TB episode, 18 (65.2%) participants received first-line treatment before screening: 10 (53.3%) received treatment for between 1 and 4 weeks, the remainder for 5-24 weeks. 13 (72%) had not had TB previously: resistance to PZA and EMB was reported in 11 (85%) and 10 (77%) respectively. Among 5/18 with previous TB, 3 (60%) were resistant to PZA and EMB.

Conclusions: Pyrazinamide and ethambutol resistance was widespread in patients with FQ-susceptible MDR-TB. Especially worrying is the prevalence of PZA resistance among patients who had no TB treatment prior to the current episode, 11/13, 85%. This is similar to the frequency of resistance among patients who received exposure during the current episode and had ostensibly received 'appropriate' treatment previously (3/5, 60%). It is possible that this exposure is inducing resistance to pyrazinamide and ethambutol during the waiting period. Finally, based on the frequency of resistance to pyrazinamide in this population we do not recommend its use in MDR treatment without a previous DST result.

SOA-504-27 Baseline and pharmacokinetic factors associated with individual outcome in the PanACEA-MAMS-TB-01 trial: lessons for regimen and trial design

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Background: individual TB treatment outcomes vary and depend on baseline characteristics and drug exposure during treatment. In the PanACEA-MAMS-TB-01 trial, 365 patients were randomized to one of the following experimental regimens for twelve weeks: 1) 35mg/kg rifampicin (R) with standard-dose INH, PZA and EMB (HZE), 2) SQ109 replacing EMB; with standard-dose RHZ, 3) SQ109 replacing EMB, with 20 mg/kg R, and standard-dose HZ, 4) moxifloxacin and 20mg/kg R, standard-dose HZ, or 5) standard RHZE. The impact of baseline factors and drug exposure on time to culture conversion on liquid media was explored.

Methods: 20 patients per arm underwent pharmacokinetic sampling after 4 weeks of treatment. Total plasma concentrations of RIF, INH, PZA were measured, and pharmacokinetic parameters calculated by non-compartmental methods. Variables were analyzed for association to the primary endpoint time to culture conversion, using a Cox proportional-hazards regression model adjusting for allocation to treatment arm; and included into the final multi-variable model if significant association with a $P < 0.05$ was found.

Results: Factors associated to faster culture conversion were lower baseline bacterial load (log MGIT TTP (days), hazard ratio (HR) 2.64, $P < 0.001$), female sex (HR 1.36, $P = 0.036$) and being recruited in South Africa (HR 2.35, $P < 0.001$), all of which were retained in the multi-variable model. No association was found for baseline BMI.

Higher AUCs for RIF, INH and PZA were significantly associated to better outcome. In a multi-variable model including those three drugs, only RIF AUC retained significance (HR 1.24 per increase of 10h*mg/l, $P = 0.006$).

Tanzanian patients in the R35 arm achieved lower RIF AUCs than South African patients (geometric means 145 and 206 h*mg/l, $P = 0.001$), and slightly lower PZA AUCs.

Conclusion: Our analysis confirms baseline bacterial load as an important prognostic factor. Among drugs measured, RIF exposure in our population was most strongly associated with outcome. In Tanzanian patients, high RIF doses have less impact on exposure than in South Africans, which partly explains longer time to culture conversion seen in Tanzanians.

SOA-505-27 Delayed tuberculosis treatment response or failure? Predictors and outcomes of month two culture non-conversion among HIV-negative patients: a Rifatox Trial Sub-study

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Background: Two months culture conversion is often used as marker of treatment efficacy in Phase 2 tuberculosis trials. However, it can vary between sites as recently shown in the Rifatox trial evaluating the safety of 10, 15 and 20mg/kg of rifampicin during the first 2 months of treatment, with a lower culture conversion in the Ugandan site. We sought to further describe the treatment response using different culture methods and to identify predictors of culture non-conversion at 2 months in this site in Uganda.

Methods: Contrary to the other trial sites (Bolivia and Nepal) using only Löwenstein-Jensen (LJ) culture at week 8, in Uganda both LJ and MGIT were used at weeks 8, 16 and 24. Week 8 culture non-conversion was based on a combination of LJ and or MGIT. Binomial regression analysis for predictors of non-conversion was used.

Results: At treatment initiation, of 100 enrolled patients, mean age was 36.2 years, 80 were males, 44 underweight, and 87 had sputum smear $\geq 2+$. Week 8 conversion rates for LJ, MGIT and LJ+MGIT for patients on 10, 15 and 20mg/kg were 51.5%, 45.2%, 60.6%; 54.6%, 41.9%, 48.4% and 50%, 40.6%, 44.1% respectively. Total conversion was attained by week 24 in all patients despite treatment arm. The difference in conversion rate between LJ and MGIT over time tends to be higher for 15 and 20mg/kg rifampicin arms compared to 10mg/kg arm. Patients in service jobs (motor-bike riders) were more likely to have not converted by week 8 (aRR = 2.4, 95%CI 0.96-5.81).

Conclusions: Despite slow conversion on both culture methods in the Ugandan site, all patients converted by the end of treatment. The type of culture method seems to influence the culture conversion more in the intervention arms than in the control arm and would require further investigation. We could not identify predictors of

slow conversion but there might be an association between patients' occupation and treatment response that would need further assessment.

SOA-506-27 The effectiveness of treatment in patients with destructive pulmonary TB depending on the mode of administration of anti-tuberculosis drugs

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Background: The aim of research was to determine the effectiveness of chemotherapy using intravenous (IV) anti-TB drugs compared with their oral administration during the intensive phase (IP) of treatment.

Methods: 130 TB patients were randomized into 2 groups: main ($n = 65$) who received isoniazid, ethambutol and sodium rifamycin IV + pyrazinamide per os and control ($n = 65$) who received all the drugs (isoniazid, rifampicin, ethambutol, pyrazinamide) orally.

Results: After 2 weeks of treatment symptoms of intoxication disappeared in 90.7% of patients of the main group (MG) and 75.0% patients in the control group (CG), $P < 0.05$. The mean duration of symptoms of intoxication in MG patients was 9.6 ± 0.7 days; in CG patients 13.4 ± 1.2 days. After completing IP, sputum conversion was found in all the MG patients and 43 (95.7%) CG patients. The average time of sputum conversion in MG was 1.6 ± 0.1 months and 1.8 ± 0.1 months in the CG, $P > 0.05$. In patients with destructive pulmonary TB, time to sputum conversion was 1.7 ± 0.1 months in the MG and 2.1 ± 0.1 months in the CG, $P < 0.05$. The average time of cavities healing in the MG was 2.9 ± 0.2 months and 3.7 ± 0.3 months in the CG, $P < 0.05$.

Conclusions: In patients with destructive pulmonary TB use of isoniazid, ethambutol and sodium rifamycin IV in the intensive phase of chemotherapy resulted in a significant reduction in terms of the disappearance of symptoms of intoxication and sputum conversion.

SOA-507-27 The efficacy of endobronchial valve installation in a complex therapy of destructive pulmonary drug-resistant tuberculosis

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Background: We conducted a randomized study of the efficacy of endobronchial valve (EbV) in the complex treatment of patients with destructive drug-resistant pulmonary tuberculosis (TB) with treatment failure. A local ethical committee, based in Novosibirsk Tubercu-

losis Research Institute, approved the study. In according to the existing hypothesis, application of the EbV will result in a selective curative atelectasis of the affected part of the lung, which contributes to early cavity closure.

Aims: To assess and to analyze the influence of the EbV in a complex anti-TB therapy on the status of the disease.

Methods: We compared the efficacy of EbV therapy in the complex treatment of patients with destructive pulmonary drug-resistant TB against the standard therapy. The cavity closure was selected as a criterion of effectiveness. In total, 102 patients with drug-resistant destructive TB were taken into the study, randomly divided on two groups: a main group of 49 patients for EbV installation and a control group of 53 patients to receive standard treatment (control group). Standard chemotherapy for all groups continued to be administered throughout the study period.

Results: 33 cases (67.3%) in the main group demonstrated cavity closure vs. 11 (20.7%) patients in the control group ($P < 0.0001$). Cavities remained in 16 cases (32.7%) in the main group and in 42 cases (79.3%) of the control group ($P < 0.0001$).

Conclusions: The application of EbV can significantly improve the effectiveness of standard chemotherapy regimens for patients with destructive pulmonary tuberculosis.

SOA-508-27 Challenges in supply of investigational medicinal products for MDR-TB clinical trials

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Background and challenges to implementation: The International Union Against Tuberculosis, through its North American affiliate Vital Strategies, is conducting a multi-center clinical trial (STREAM) to evaluate shorter treatment regimens for multidrug-resistant tuberculosis (MDR-TB) by comparing different combinations of generic and proprietary medicines with the current standard World Health Organization recommended treatment. Uninterrupted availability of investigational medicinal products (IMPs) is crucial for successful implementation of such a clinical trial. Supply chains for IMPs are complex. These products are highly regulated, their cost is often substantial and they require rigorous accountability. Other limitations include compulsory temperature monitoring, batch management and restricted shelf life. Supply chains for IMPs for MDR-TB trials have unique specificities like sourcing complexity, procurement challenges, lengthy lead times, laborious stock management and a need for daily dispensing pack preparation.

The majority of clinical trials involving drug interventions require supply of up to three IMPs for a limited period of time. The STREAM trial requires availability of nine IMPs during a treatment period up to 40 weeks.

Intervention or response: Risk assessment identified potential risks and classified them into priority groups

according evaluated harm severity and occurrence possibility. Preventive measures were identified and implemented.

Results and lessons learnt: The study identified 20 potential risks and classified them into 7 groups according to severity and occurrence possibility with catastrophic being the most urgent to address and marginal the less urgent. Although requirements to obtain regulatory approval for clinical trials are clearly defined, certain documents on IMPs, notably generic medicines used in MDR-TB treatment, are non-existent and cannot be provided. This was considered as a risk with potential catastrophic consequence on trial approval. Similarly inappropriate stock management system resulting in stock outs and expired stocks would have catastrophic consequence on IMPs availability to study participants. Addressing these risks through education and discussion with study partners was considered to be a priority risk mitigation strategy. Other risks were addressed similarly.

Conclusions and key recommendations: Successful identification of risks and their management requires advance planning, sufficient human and financial resources and strong network of partners for ensuring uninterrupted timely availability of IMPs to study participants.

SOA-509-27 Tuberculosis clinical trial activity on the African continent: analysis of tuberculosis trials registered on the Pan African Clinical Trials Registry

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Background: A third of tuberculosis (TB) related deaths occur in Africa. Among people living with HIV, at least one in four deaths can be attributed to TB, often in resource-limited settings. Clinical trials constitute an essential research tool to evaluate various treatment, prevention and implementation interventions for TB. The Pan African Clinical Trials Registry (PACTR), the only African member of the World Health Organization's (WHO) Primary Registry Network, provides a venue and support for registration of trials conducted in Africa. PACTR contributes to WHO's International Clinical Trial Registry Platform's (ICTRP) central database of clinical trials, and also to initiatives to strengthen regulatory and research frameworks.

Objective: To describe TB trials conducted in Africa and registered on PACTR

Methods: We searched PACTR for randomised or controlled clinical trials evaluating interventions for TB. Data extraction included the number of trials, their location, intervention studied, principal investigator's (PI) location, participant age range and funder. Descriptive analysis was run in MS Excel.

Results: There are 661 studies registered on PACTR between June 2009 and March 2016, with 53 trials

reporting planned or ongoing TB research. Twenty-seven PACTR trials explored treatment, ten diagnosis, five prevention trials included two vaccines, five education and counselling, and four supportive care interventions. Sample sizes range from 12 to 27 000. Twenty-four trials were single-centred in 11 countries; 29 multi-centre trials in 13 African countries with 41 African PIs and 12 from Europe and USA. Eighteen trials received funding from the European and Developing Countries Clinical Trials Partnership (EDCTP); none were industry funded.

Conclusions: The increase in PACTR registrations make the registry a tool for regulatory and funding bodies to monitor the changing TB trial landscape in Africa; it is also a resource for TB specialists to determine gaps in research, or potential collaborators. PACTR and WHO-ICTRP are valuable resources for systematic review authors to identify ongoing African TB trials.

02. 'We can work it out': understanding and preventing diagnostic treatment delays

SOA-511-27 The social determinants underlying tuberculosis diagnostic delay: a mixed methods study

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Background: Early detection and diagnosis of TB remains a major priority for global TB control. Few studies have used a mixed methods approach to investigate the social determinants contributing to diagnostic delay and none have compared qualitative data collected from individual, community, and health-system levels. We aimed to characterize the social determinants that contribute to diagnostic delay among persons diagnosed with TB (PDTB) living in resource-constrained districts of Lima, Peru.

Methods: Data were collected in 19 districts of Lima between May and October 2015. Semi-structured interviews with PDTB ($n = 105$) and their family members ($n = 61$) explored health-seeking behaviors, community perceptions of TB and socio-demographic circumstances. Focus groups ($n = 7$) were conducted with healthcare personnel working in the National TB Program (NTP) and explored the relationships and attitudes between staff, PDTB and the NTP. All interview data were transcribed and analyzed using a grounded theory approach. Factors associated with diagnostic delay were analyzed.

Results: The median delay between symptom onset and the clinic visit that led to the first positive diagnostic sample was 57 days (interquartile range 28-126). In negative binomial regression adjusted for age and sex, increased delay was associated with older age; female sex; lower personal income prior to diagnosis; living with fewer people; having more visits to health posts prior to diagnosis; and initially visiting a private clinic as opposed to a public or employer insured health facility (all $P < 0.05$). In qualitative analysis, the great majority of PDTB distrusted the public health care system and sought care at public health posts only after exhausting all other options. It was universally agreed that PDTB faced discrimination by both the public and healthcare personnel. Self-medication was reported as the most common initial health-seeking behavior due to the speed and relatively low-cost of treatment in pharmacies. Most PDTB perceived their illness as a simple cold that would pass.

Conclusions: Diagnostic delay is common, prolonged and greatest among older, low income, socially isolated women. More and improved human and material resources are required to promote TB case-finding initiatives, reduce TB-associated stigma and address the social determinants of diagnostic delay.

SOA-512-27 Perceived barriers and facilitators of isoniazid preventive therapy among people living with HIV in South Africa

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Background: Despite the World Health Organization's recommendation that all people living with HIV (PLWH) receive isoniazid preventive therapy (IPT), the uptake of IPT has been poor worldwide. We sought to quantify patients' perceptions of the barriers and facilitators to preventative therapy and to compare these across those who are and are not currently receiving IPT.

Methods: Data was derived from a cross-sectional survey of adults (≥ 18 years) with a recent HIV diagnosis (< 6 months) across 14 public primary health clinics in Matlosana, South Africa. Potential barriers and facilitators of preventive therapies ($n = 16$) were identified from a literature review and prior qualitative research. Patients' perceptions were assessed using best-worst scaling, where respondents evaluated repeated sub-sets of the factors and identified which was the greatest barrier (scored -1) and facilitator (scored $+1$). These were averaged, resulting in a score from -1.0 (largest possible barrier) to 1.0 (largest possible facilitator) and compared across current IPT status using Student's t -test.

Results: Among 342 patients surveyed from January 2014 to August 2015, 114 (33%) were on IPT. The median age was 34 years (IQR 27-41), 64% were women, and the median time since HIV diagnosis was

28 days (IQR 9-79). Overall, the strongest facilitators were a high standard of life among PLWH (0.35 ± 0.01) followed by trust in healthcare providers (0.33 ± 0.01). Beliefs about perceived barriers and facilitators varied significantly by IPT status. Among those on IPT, the perceived likelihood of avoiding illness was rated much lower ($P < 0.0001$) while fear of HIV disclosure to family and side effects of medications were rated less negative ($P < 0.0001$).

Conclusions: Creating an environment that ensures patient confidentiality and discussion of potential side effects may enhance IPT uptake. These results point to concerns that must be addressed if IPT is to be delivered in a patient-centered fashion among PLWH.

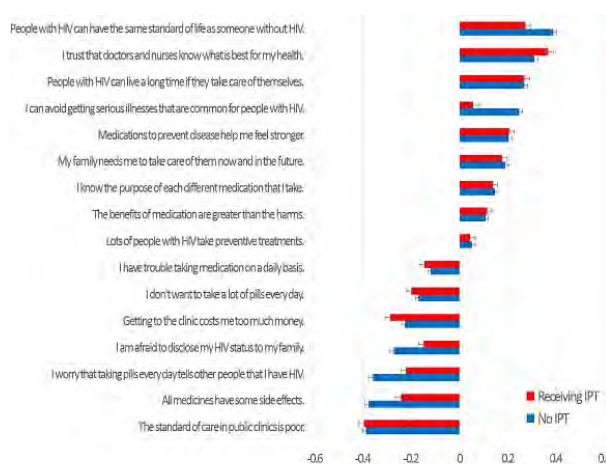


Figure 1. B-W score of 16 different barriers and facilitators among newly diagnosed HIV-infected individuals by IPT initiation. Error bars represent standard errors. All B-W scores range from -1 (worst) to 1 (best).

SOA-513-27 Cultural adaptation and validation of the tuberculosis-related stigma scale in Brazil

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Background: Tuberculosis-related stigma (TB) has aroused interest in different regions around the world. The patients' behavior deriving from social discrimination has contributed to diagnostic delays and treatment abandonment, resulting in an increased number of tuberculosis cases and in drug resistance. The identification of populations affected by stigma and its measuring can be assessed by means of validated and reliable tools developed or adapted to the target culture. The objective in this study was to culturally adapt to Brazil and obtain the psychometric properties of the tuberculosis-related stigma scale, constructed and validated by researchers in southern Thailand.

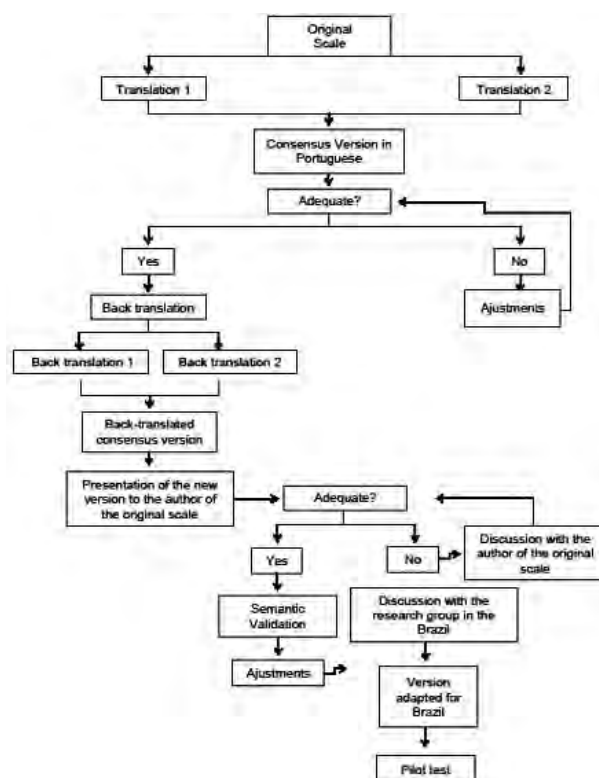
Methods: A quantitative methodological research was undertaken, divided in three phases: translation and back-translation of the items; semantic validation, involving 17 subjects; pilot test, including a sample of

60 Brazilian patients under TB treatment, recruited from referral outpatient clinics in the city of Ribeirão Preto, São Paulo, Brazil (Figure). In the three phases, statistical analyses appropriate for the instrument validation process were applied, based on the method of the DISABKIDS® group.

Results: In the translation and back-translation process of the items, few terms were adapted to the target culture. The semantic validation showed the participants' good acceptance of the scale, which was considered good and consisting of items easy to understand. In the pilot test, no floor and ceiling effects were found. The reliability and internal consistency showed Cronbach's alpha coefficients of 0.554 and 0.525, respectively, demanding the recruitment of new participants. The multitrait-multimethod analysis for convergent validity showed scores superior to 0.30 for nine items on the scale.

Conclusions: The preliminary results of the scale indicate the appropriateness of the equivalences between the original and Brazilian version, in view of the linguistic and cultural variations assessed. Nevertheless, the initial psychometric properties indicate that the scale needs to be tested with a larger number of participants in the Brazilian context.

Figure Flow chart of cross-cultural adaptation



SOA-514-27 Delays of tuberculosis diagnosis in patients from a tuberculosis referral hospital in urban southeastern China

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Background: China has amongst the largest epidemic of drug susceptible and resistant tuberculosis cases globally. We investigated factors associated with total delay in tuberculosis diagnosis and locations where patients reach out to receive care from a large tuberculosis, referral hospital in Nanjing, China.

Methods: We conducted a retrospective cohort study among tuberculosis patients who initiated anti-tuberculosis treatment three months prior to reaching out to the health care system. Patient information regarding the time and locations visited while seeking care were collected through face-to-face interviews. Crude and adjusted cox proportional hazard ratios (HR) of factors associated with time and number of steps to diagnosis were calculated.

Results: Of 225 recruited tuberculosis patients, 46 (20%) were diagnosed radiologically and were excluded. After exclusions, 179 laboratory-confirmed patients were included in final analysis. The mean days and steps to diagnosis was 50.3 and 2.2. Female patients (HR 0.71, 0.52–0.97) or who contacted a health care provider two weeks after becoming symptomatic (HR 0.42, 0.30–0.57) were significantly associated with a slower time to diagnosis. Public hospitals were the most commonly visited healthcare institution and repeated visits to them were common before referral to a tuberculosis-specific hospital.

Conclusions: In a referral hospital in urban China, we found that female tuberculosis patients took significantly more time to reach diagnosis than males. In addition, patients often cycled in public hospitals for multiple visits before reaching final diagnosis. Public hospitals should encouraged to refer potential tuberculosis patients as soon as possible to avoid nosocomial transmission.

SOA-515-27 Predictors of delay in seeking tuberculosis care in South Kivu Province, Democratic Republic of the Congo

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Background: Tuberculosis (TB) remains a global health threat, especially in sub-Saharan Africa including the Democratic Republic of the Congo's South Kivu Province where the notification and success rates in 2014 were 57/100 000 and 80%, respectively. We aimed to investigate predictors for delay in seeking TB care in this setting.

Methods: We conducted in-depth interviews at 23 centers for TB diagnostics and treatments from January to March 2015. Descriptive data were summarized using means and proportions. The χ^2 test was performed to compare proportions.

Results: Eighty-two patients on TB treatment were interviewed. Mean age: 40 years old and 40 % were females. Delay (range) in seeking care was documented at 3 months (1–9 months). Predictors for delay in seeking TB care were male gender (OR = 0.33; 95%CI 0.12–0.94), living in rural setting (OR = 2.48; 95%CI 0.88–7.04) and low education level (OR = 2.6; 95%CI 0.93–7.38). Patients who were older (OR = 1.18; 95%CI 0.45–3.11), highly educated (OR = 1.20; 95%CI 0.45–3.22), or living in an urban setting (OR = 2.48; 95%CI 0.88–7.04) were more likely to seek TB care and report symptoms such as chronic cough.

Conclusion: Delay in seeking TB treatment was prevalent in this population, especially for males, rural living patients and poorly educated patients. Specific causes for delay in seeking TB treatment and interventions to address them are sorely needed in this setting.

SOA-516-27 'Anything to do with TB is dangerous': exploring barriers to uptake of household TB screening intervention in Blantyre, Malawi

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Background: A household randomised trial was piloted in Blantyre, Malawi, as an alternative model for TB screening in order to investigate feasibility and acceptability of a patient-delivered approach. During trial implementation, preliminary analysis revealed that 54.1% (251/464) of eligible TB patients declined participation in the trial.

Methods: Forty two in-depth interviews were conducted with patients (32 participants) and trial workers (10) to investigate reasons why eligible patients failed to participate in trial. Content analysis aided by NVIVO 10 software, analysed the qualitative data.

Result: Barriers were identifiable at patient, community, health systems and trial implementation levels. Patient-level barriers included poor health condition of patient and perceived financial burden associated with hospital visits if contacts were in need of medical care. Disclosure of TB and HIV status to community members subsequently attracted associated community stigma.

At health systems level, eligible patients were concerned about inability to guarantee their privacy and confidentiality due to congestion and limited space with TB services in Malawi. Relating to research set up, poor communication and approach during screening process by study team members (who included routine TB officers) was identified as a barrier to eligible participants.

Conclusion: The acceptability in household level TB screening interventions may be lower than anticipated due to financial costs, social stigma especially if a household visit is included. Lack of privacy within the Malawi programme may exacerbate these concerns. Screening approaches that involving patient-delivered should be re-evaluated for effectiveness and acceptability in a range of setting in consideration of these barriers.

SOA-517-27 Facilitators and barriers in TB treatment seeking and retention in care: patient and provider perspectives in South Africa

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Background: Delays in seeking treatment for tuberculosis (TB), and lost to follow-up, are challenges faced by national TB programs worldwide. These challenges particularly affect resource-limited settings plagued by high TB incidence. This qualitative study explores barriers and facilitators for seeking prompt diagnosis and treatment, and for retention in care.

Methods: Between December 2015 and June 2016, open-ended, semi-structured interviews were conducted with

adult TB patients (≥ 18 years old), as well as public and non-public healthcare providers involved in TB care, in Cape Town, South Africa. Purposive sampling was used to recruit participants from diverse backgrounds. Qualitative content analysis identified themes emerging from interviews. To date, participants were recruited from two public TB clinics and one public hospital, including: 10 TB patients (with both drug-susceptible and drug-resistant disease); 3 community care workers (CCWs); 2 TB nurses; and 1 TB counsellor. Six patients were black South Africans (four were male), and four were coloured South Africans (half were male). Aged 21–49 years, and delay in seeking diagnosis ranged from 2 to 6 weeks. All healthcare workers were black females.

Results: Male patients were more likely to express concern over poor attitudes from healthcare providers than female patients, which affected motivation to complete treatment. Patients with multidrug-resistant TB (MDR-TB) presented views that providers treated them more poorly than non-MDR-TB patients, and they had longer wait times. Many patients reported crime and violence as deterrents to seeking and continuing treatment at clinics, and the need for medication to be provided outside clinics. Healthcare providers often reported heavy workloads and staff shortages as challenges to proper follow-up of patients. Both patients and providers reported the need for more community outreach to provide education on symptoms and care of TB, as well as sufficient follow-up of existing patients. **Conclusions:** Barriers within communities most affected by TB, such as crime and violence, are disabling patients from properly seeking care for TB. Outreach initiatives providing education and treatment to people living in these communities are greatly needed in order to increase TB diagnosis and treatment completion rates.

SOA-518-27 A pilot study to investigate the relationship between illness perception and clinical characteristics in patients with pulmonary tuberculosis in South Korea

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Background: Illness perceptions have important associations with outcomes in a wide range of diseases, and vary with cultural, ethnic and socio-economic differences. South Korea is a country with an intermediate burden of tuberculosis (TB). Illness perception of TB is known to influence medication adherence, which is essential for successful treatment outcome. The aim of this study is to investigate relationship between illness perception and clinical characteristics in patients with pulmonary TB in South Korea.

Methods: Thirty patients with pulmonary TB (mean age 53.2 ± 18.6 ; males 70.0%) were enrolled in this study from July 2015 to February 2016. The illness perception was measured by using brief illness perception questionnaire (BIPQ). The BIPQ was completed by patients and

collected within 2 months of initial diagnosis. TBscore, which assesses mortality and treatment failure risk of TB patients, was adopted. Clinical characteristics, such as age, sex and sputum AFB smear were also collected.

Results: The over BIPQ score (34.4 ± 15.0) was in concordance with the clinical TB score (Pearson's correlation of 0.608). Among 8 items of BIPQ, the mean score of treatment control was the highest (7.6 ± 2.2), and that of identity was the lowest (3.5 ± 3.1). Patients with a TB score ≥ 4 had a significantly higher total BIPQ score than those with TB score ≤ 3 (49.7 ± 15.2 vs. 29.7 ± 11.6 ; $P = 0.001$). Patients with two or more symptoms had a significantly higher total BIPQ score than those with one symptom or without any symptoms (30.3 ± 14.1 vs. 42.5 ± 13.9 ; $P = 0.033$). The total BIPQ scores were not different in regard to age, sex, and sputum AFB smear. Patients with age ≥ 65 years had higher score for treatment control than those with age < 65 (8.3 ± 2.0 vs. 5.9 ± 1.7 ; $P = 0.004$). Patients stated that smoking and patient's unhealthy behavior were the two most important causes, and only one patient ascribed the illness to germ.

Conclusions: TB patients believed in the treatment, but were unsure about the illness identity. Further efforts are needed to make TB less mysterious and confusing. Careful and close follow-up is necessary for patients with more recognized symptoms and signs. Proper education about tuberculosis should also be accompanied.

03. Methodologies and models for TB education and training

SOA-519-27 Health education and focus group discussion to increase knowledge, motivation and medication adherence among patients with tuberculosis

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Background and challenges to implementation: Tuberculosis is still a major health problem in Indonesia. The preliminary study in one lung center hospital has shown that 70% of patients stopped taking medicine due to reduce symptoms. The preliminary study identified patients' lack of knowledge, including: understanding impact of incomplete treatment (30%), prevention of TB infection (50%), side effects of TB drugs (80%) and length of TB treatment (20%). Therefore, it is important to increase the knowledge, motivation and taking medicine compliance of patients with TB.

Intervention or response: The health education was held in lung clinic of RSUP Persahabatan in November and December 2015. 30 respondents of outpatients, with 43.3% patients were taking intensive treatment phase and 56.7% respondents were in advanced treatment phase were involved in the intervention. The health education was held using focus group discussion method, in which each group consisted of 6 respondents. The discussions was initiated by sharing experience of TB patients related to the treatment they were taking. Respondents shared their symptoms, obstacles, how to solve problems during undergoing the treatment. Following this, the patients were given health education by the facilitators regarding the disease and tuberculosis treatment.

Results and lessons learnt: The patient's knowledge and motivation increased, the knowledge score average (from 9.30 into 10.67) and the motivation score (from 20.73 into 22.80). Based on statistical test, it can be concluded that there is significant difference between knowledge score before and after health education ($P = 0.000$) and there is significant difference between motivation score before and after health education ($P = 0.000$). The patients medication adherence also increased, where the patients went back to the hospital for purchasing medicine after 2 and 4 weeks of the intervention. It is proved by the increased. This study shows how important the health education which focuses more on small group discussion is, so patient can mutually share their experience and communicate their symptom as well as obtain health education intensively.

Conclusions and key recommendations: It has been shown that health education using focus group discussion method increased knowledge, motivation and medication adherence of respondents.

SOA-520-27 Use of mobile technology to reach the unreached with information on TB: experience from six states in India

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Background and challenges to implementation: Out of 3.6 million unreported or missing tuberculosis (TB) cases worldwide around one million are estimated to be in India. Although Advocacy Communication and Social Mobilization (ACSM) efforts have been made for a long time, there is a hesitation among chest symptomatic patients to seeking TB related information, diagnosis and treatment in person due to feared stigma and prevailing unfavourable social norms.

Intervention or response: To address this challenge, Project Axshya involved a call centre to pilot a Toll-Free Helpline in six states with an objective to link TB symptomatic patients to a platform which can provide accurate reliable information on TB disease, referral linkages to TB diagnostic and treatment services in a

confidential manner. Trained call agents provide information on TB, clarify its signs and symptoms, and provide details of diagnostic services close to the caller and referral linkages to TB treatment services. Regular refresher training, quality assessments and standard operating procedures maintains the quality of services provided through the Helpline. The Helpline number is promoted through below the line and above the line ACSM activities in the project states.

Results and lessons learnt: From April 2014 to Feb 2016, 47 530 calls were received in the Axshya Helpline. Of these, 86% of the callers were male and 14% were female. Around 60% of the callers called the Helpline to seek information on TB Diagnostic services, which are linked to Designated Microscopic Centres (DMC) close to their locations. Around 10% of already-affected patients sought information on TB treatment, MDR-TB and were counselled on treatment compliance. The remaining 30% callers were counselled on TB signs and symptoms and were linked to RNTCP centres.

Conclusions and key recommendations: Looking at the response to the Axshya Helplines in six pilot states, it is estimated that there is high demand for the platform to provide TB information in a confidential manner. Based on the learnings from the Axshya Helpline, the Central TB Division (CTD) in India is looking at scaling up the Helpline across all states.

SOA-521-27 Implementing the ECHO Telehealth Model to strengthen nurse case management and improve TB patient care outcomes

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Background and challenges to implementation: The ECHO model is an evidence-based educational intervention that strengthens knowledge and clinical practice through videoconferencing, case-based learning, promotion of best practices, and outcome monitoring. The New Mexico TB Program (TBP) in collaboration with the University of New Mexico ECHO Institute has adapted the ECHO model to ensure effective nurse case management (NCM) of all active TB patients in the state by empowering public health nurses (PHN) with knowledge and skills. The TBP aims to strengthen patient outcomes through a community of practice and learning for PHNs.

Intervention: The NM Department of Health TB tele-ECHO clinic convenes PHNs from across New Mexico on a monthly basis via a video network to review all active TB cases [average 20 month/50 year]. Short 15-20 minute didactics address high priority clinical and programmatic topics and complement the case-based learning. The goals are to strengthen NCM skills,

professional learning development, and program quality improvement. A self-efficacy survey was completed at baseline and again at 7 months to evaluate the nurses perceived levels of competence in providing NCM. Anonymous feedback is collected monthly after each TeleECHO session and adjustments made to the program.

Results and lessons learnt: NM TBP launched its first TB TeleECHO Clinic on 20 April 2015. 21 PHNs presented 43 unique patients with active TB for a total of 161 presentations in the first 11 months; there have been more than 240 unique participants from across the United States and Mexico. A total of 586 CMEs have been awarded. Self-efficacy survey results at month seven showed an increase in the confidence of the PHNs to provide quality patient care in all categories. While some find the time commitment of 3 hours per month challenging, attendance remains consistently strong with an average of 16 PHNs attending each session.

Conclusions: This public health/academic medical center collaboration has enhanced NCM practice by creating a supportive community of practice and learning. The program offers an example of an efficient and cost-effective model for continuous public health workforce education and a platform for routine standardized monthly cohort review.

SOA-522-27 Effects of motivational interviewing on treatment adherence of people affected by TB in the Philippines

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Background: Non-adherence remains as one of the barriers in eliminating TB in the Philippines. TB adherence declines due to loss of motivation. Motivation affects self-efficacy to treatment adherence. Moreover, motivation has significant psychological (75%) and physiological (72%) effects on diseases. Hence, this study aims to examine the effects of adapted Motivational Interviewing (MI) to enhance the treatment adherence of people affected by TB.

Methods: The study utilized an experimental, pre-post test design. Thirty people affected by TB were randomly assigned to control and experimental groups using multistage cluster sampling. The experimental group received four sessions of 30-minute nurse delivered adapted MI weekly for one month, while the control group received standard health education. MI is a counseling style that used specific questions to direct behavior change by expressing empathy, developing discrepancy, rolling with resistance and supporting self-efficacy. Adherence was measured using multi-method approach combining subjective and objective measurement. Subjective measurement involved the use of Medication Adherence Self-Efficacy Scale (MASES) before and 2 weeks after the intervention. A panel of experts reviewed the MASES to ensure face and content validity, and the instrument was subjected to internal consistency with a Cronbach alpha of 0.80. Objective

measurement involved the use of sputum AFB microscopy done before and 1 month after the intervention.

Results: Independent *t*-test revealed there was a significant difference in the medication adherence self-efficacy scores ($P = 0.036$) and sputum AFB count ($P = 0.047$) between two groups before and 2 weeks after the intervention. The mean pre and posttest medication adherence self-efficacy scores of the experimental group (2.32–2.97) is higher compared to the control group (2.31–2.32). Moreover, the mean pre and post test sputum AFB count of the experimental group (1.6–0.07) is lower compared to the control group (1.61–0.4).

Conclusions: Knowledge about the disease and its treatment combined with motivation can increase self-efficacy of people affected by TB to treatment adherence. Motivational Interviewing as an adjunct to the standard health education is effective in enhancing treatment adherence of people affected by TB in the health center. Consequently, decreasing the number of *M. tuberculosis* in the sputum microscopy.

SOA-523-27 Implementation of international workshops for building technical capacity within NTPs using the TIME model

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Background and challenges to implementation: The potential of mathematical modelling for guiding decision-making has yet to be fully utilised by National TB Programmes (NTPs) to support strategic planning. Low- and middle-income countries often lack resources and technical capacity to build mathematical models while most existing TB models are designed for academia, making them inaccessible to NTPs.

Intervention or response: We implemented international training workshops with the TIME model to build capacity within NTPs, and to facilitate local ownership of modelling results to support TB strategic planning. Two cohorts were included, covering three countries in South-East Asia (Indonesia, Vietnam, Myanmar) and six in sub-Saharan Africa (Nigeria, Ghana, Zambia, Malawi, Tanzania, Ethiopia). Each cohort participated in two workshops, with remote support during the inter-workshop period. Each country included at least two participants nominated by the NTP. The cohorts received hands-on practice with TIME and training on reviewing country-specific data, identifying and modelling epidemiological impact of policy questions, as well as effective communication of results and assumptions to policy-makers. A pre-calibrated model with instructions guiding them towards exploring the country's epidemiology and modelling the impact of interventions was provided. Participants then used local data to calibrate a TIME model to their setting.

Results and lessons learnt: Participants completed the training cycle and led on applying the model to address

country-specific policy questions and communicated findings to local policy actors, such as national ministries. NTPs reported that they will be dedicated to continue applying TIME in their country context to address local policy questions to support national strategic planning within their funding cycle.

The workshops proved to be a good opportunity to begin the data strengthening process. Challenges of implementing these trainings include limited capacity to expand training delivery coverage and developing an optimal remote support system that is tailored to the diverse political constraints of attending countries.

Conclusions and key recommendations: These workshops are a feasible approach to building technical capacity within NTPs to provide them with the necessary skills to model their TB epidemic and explore the impact of interventions of interest using the TIME model.

SOA-524-27 National remote TB consultation and training platform: an innovative way to ensure sustainable capacity building for TB hospitals in China

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Background and challenges to implementation: China is now in a transition period to shift TB diagnosis, treatment and management from CDC to hospitals. There is a huge need on capacity building and technical support to TB hospitals especially peripheral hospitals at county and prefecture levels. However, conventional face-to-face training workshop is costly and time determinant and cannot meet the needs for long term, systematic, sustainable training.

Intervention or response: With rapid development and wide use of internet technology, the Clinical Center on Tuberculosis, China CDC (CCTB) developed an internet based 'National Remote TB Consultation and Training Platform' with support from Janssen, Lilly MDR-TB partnership and other partners. CCTB invites national experts to provide regular webinar training on standard TB care to all participating hospitals, organizes ad hoc on-line training or workshop upon special requirements. The participating hospitals can also raise application to the platform asking for expert consultation to the refractory TB cases in their hospitals.

Results and lessons learnt: The platform now covers 128 TB hospitals in 31 provinces of China. From 2013 to 2015, 165 webinar trainings and 25 ad hoc meetings have been conducted, 68 cases were discussed, and nearly 3000 doctors (times) joined training. 10 selected classic training lectures were developed into VCD for more widely and continuous use. This innovative way to deliver training and technical support is highly recognized and appreciated by TB hospitals.

Conclusions and key recommendations: Compare to conventional training, the webinar training through the

platform is more convenient to organize, more flexible and easier for doctors to attend, and much cheaper. This makes possible for a long-term, systematic, sustainable capacity building. It also allows very flexible and timely technical support to needed TB hospitals. The China National TB Program is planning to include this system into national training scheme, and the end users of this platform are expected to have a big increasing in coming years. CCTB needs to further analyze the needs on training and technical support from difference TB hospitals and conduct more targeted training and support. Also, an assessment on the effectiveness of platform training should be conducted.

SOA-525-27 Developing practical tools to train pharmacists in TB care and control in India

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Background: Since year 2006, community pharmacists are being trained for TB Care and Control, by Indian Pharmaceutical Association (IPA) jointly with Revised National Tuberculosis Control Programme (RNTCP) and Chemist Association. IPA first started working in Mumbai and since 2010, with support of Lilly MDR-TB Partnership, spreading this public private mix model in various parts of the country.

Methods and results: Initially, IPA used training module for Community DOT Providers developed by RNTCP and focus of the training was to only develop pharmacist as DOT providers. As the pilot trainings progressed, and partnership started evolving, IPA recognized additional tasks which pharmacists can perform. After discussion with the RNTCP and continuous dialogue with few active pharmacists, IPA defined various other roles of pharmacist such as case referral of chest symptomatic, community awareness, patient counsellor and rational use of antibiotics. IPA worked on details of patient counselling points. Guidelines for 'whom to refer' and 'where to refer' were developed. Referral slip for Sputum test was developed which was similar to RNTCP. After studying the Drug Act and after discussion with Food and Drug administration, various required formats were developed to enable pharmacist to act as DOT provider by stocking free anti-TB medicines of RNTCP. The exact training protocols and training contents were decided. Training included discussion on TB Basics, Role of Pharmacist, Introduction to DOTS protocols, linking with field staff, question/answers, pre/post tests, distribution of ACSM material and filling of necessary forms. IPA developed complete training package incorporating all above information and various formats, submitted it to Central TB Division (CTD), Ministry of Health. CTD reviewed, modified the contents and in year 2012, the Training Module was published as joint publication of CTD and IPA. It is made available on www.tbcindia.nic.in Several NGOs translated it in regional languages and this module is now widely used in India for training of pharmacists.

Conclusion: Training Module has been proved effective and practical tool for training of pharmacists pan India. While developing the training tools, it is essential to study the potential of model, understand ground realities, legal requirements and work culture of the proposed participants.

SOA-526-27 Impact of training nurses on TB/MDR-TB in China

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Background and challenges to implementation: China has the third highest burden of TB after India and Indonesia. Nurses play an important role in the next 20 years of TB control according to the WHO End TB strategy. Nurses can have a great impact on global TB control by providing and advocating for patient-centered care.

Intervention or response: The International Council of Nurses (ICN)-Lilly TB/MDR-TB Project is working to strengthen the global nursing capacity in the prevention, detection, care and treatment of TB and M/XDR-TB through a Training for Transformation (TFT) initiative. Each nurse trained is required to train an additional 20 nurses and allied health professionals.

Results and lessons learnt: Since 2009, TFT programs have been run in China and 204 TB nurses working mainly in the TB and HIV fields were trained. Nineteen of them were asked to answer questionnaire about impact of TFT on their nursing practice. These nurses trained 4163 others including: 1926 nurses, 146 doctors, and 1785 allied health workers, nursing students and community staff in their hospitals and community members. Twelve (75%) of them developed health education materials, such as leaflets, brochures and handouts. Nine of them reported an increase in people presenting with symptoms of TB. Following the training, 12 (75%) of them implemented changes regarding how sputum is collected and transported to the lab, 13 (81%) of them have seen improvements in the quality of sputum samples (e.g., fewer rejections from the lab), and 7 (44%) of them reported the turnaround time for sputum results has decreased. Ten (63%) implemented changes in their practice to improve patient treatment adherence and reported improved adherence. Fourteen (88%) reported improving psychosocial and emotional support provided to patients and 15 (94%) reported improved education for patients and their family members. Thirteen (81%) of them now provide surgical masks to coughing patients and 12 (75%) improved ventilation in their setting.

Conclusions and key recommendations: The ICN training provided much needed knowledge on all aspects of TB/MDR-TB, but just as important, it empowers and gives nurses the confidence to improve their practice, to negotiate with superiors and colleagues to make improvements.

SOA-527-27 Mass media ACSM improves health-seeking behavior for TB in Nigeria

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Background and challenges to implementation: Nigeria ranks 2nd of the 22 high burden TB Countries with a TB incidence of 322 and prevalence rate of 355 per 100 000 people. The TB case detection of Nigeria is at a low of 15%. The 2012 Nigeria TB Knowledge, attitude and Practice (KAP) survey estimates the population awareness of TB at 21%. Poverty, illiteracy and poor health seeking behavior are known risk factors in the Nigeria TB situation. FHI360 used USAID resources to engage the mass media for strategic TB Advocacy, Communication and Social Mobilization (ACSM) towards improving health seeking behavior of individuals towards TB services in 5 states of Nigeria.

Intervention or response: This was a cross sectional descriptive survey. Baseline assessment of TB knowledge, attitude and practice (KAP) were conducted through random sampling of the general population in 5 states. Nine commonly tuned media outlets were engaged for daily airing of messages related to TB disease, diagnosis, treatment and referral. Data on persons with TB and those identified with features of TB were counted from the TB treatment and suspect registers of the states in the two quarterly reports six before and six months after the intervention. A follow-on KAP assessment was repeated randomly in the population after 6 months of the intervention. KAP estimates were summarized with percentages.

Results and lessons learnt: An average of 70% of the respondents admitted to have heard about TB over the media of which 90% admitted that they understood the messages broadcasted. 50% of the respondents believed TB treatment is free. An increase in TB case finding of 2.6% (pre = 10 901; post = 11 192; $P = 0.71$) and TB suspects reported in the facilities of 27.1% (pre = 28 614; post = 38 756; $P < 0.001$) was recorded following the broadcast.

Conclusions and key recommendations: The results indicate a significant increase in TB suspects following the broadcast. However, the TB ACSM needs to be strengthened to increase public awareness of free TB treatment in public health facilities. This will go a long way to improving the health seeking behavior for TB in Nigeria.

SOA-528-27 Innovative e-learning methodologies using digital technology for TB-HIV: a digital India campaign

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Background: Increasing access to information communication technology has provided opportunities for range of training methodologies to respond to the demands of knowledge needs, prepare staff with skills and competencies for the effective service delivery. This paper highlights use of digital technologies for TB and HIV training with shift from conventional trainings.

Intervention: With the support of IL&FS, an 'e-learning module for HIV TB' was developed and an e-book on 'Guide to Supervision, Monitoring and Evaluation of TB HIV' supporting android based mobile application is also made available. Structured Online 'distance learning program for HIV TB' are planned and conducted with support of ITECH India. Online 'Video dialogues' are conducted to address the issues and challenges related to HIV TB with district and provincial staff. Google groups, Facebook, WhatsApp, Skype are used as discussion platforms to adapt to the needs of the staff. Online community also provides them the opportunity to learn on important topics. Recorded links of session are shared with all and uploaded on India HIV AIDS resource centre.

Results and lessons learnt: Use of digital learning platforms is more interactive and effective communication process and facilitates a participatory learning and also the development of online learning communities. Online training is effective in supporting providing knowledge with limited resources and is also user friendly considering the time, travel and loss of working hours for conventional trainings. Barriers noticed for use e-learning included lack of understanding of why and how technology, deficits of skills, motivation, institutional cultural clash between conventional training methodologies.

Conclusion: Investments in e-learning methodologies, strategic use of ICT with a view to reach different target groups, overcome the barriers of time and place to learn, creating new opportunities for collaborative learning skills is needed. There is need to use digital technology as a transformative tool in training.

04. SAD to have TB: smoking, air pollution and vitamin D

SOA-529-27 Prevalence of cigarette smoking among patients with tuberculosis in Southern Namibia K Husselmann,¹ F Mavhunga,² J Ndile,³ A Vermeulen,¹ N Ruswa² ¹Ministry of Health & Social Services, Karasburg, ²Ministry of Health & Social Services, Windhoek, ³Ministry of Health & Social Services, Keetmanshoop, Namibia. e-mail: karin.husselmann@yahoo.com

Background: Globally, the smoking of tobacco products (cigarette, pipe and other tobacco products) has been linked to the development of tuberculosis. Karasburg is a sparsely populated arid district in Southern Namibia with 18 604 inhabitants and a TB case notification rate of 618/100 000 (2014). Tobacco smoking among TB patients has not been quantified in Namibia, but Southern Namibia has a higher prevalence of smoking than elsewhere in Namibia. This assessment aimed to compare the prevalence of smoking among bacteriologically confirmed TB cases (cases) to that among patients admitted for non-TB conditions (controls) in Karasburg District Hospital.

Methods: A case-control study design was employed. Hospital records of patients admitted between January 2014 and December 2015 were reviewed, and 115 cases and 165 controls matched for age and sex were included. The age range was 15–89 (median age for both cases and controls was 36 years). Smoking history, alcohol consumption, HIV status and other demographic information were collected from patient records.

Results: From the 115 confirmed cases, 98 (86%) had smear positive TB, while 16 (14%) were smear negative but diagnosed through Xpert MTB/RIF. 89 (77%) of the TB cases had smoking history documented. The prevalence of smoking among TB cases was 37% (33/89), compared to 29% (41/142) of the controls. Of the TB cases who smoked, 3 (12%) smoked more than 30 cigarettes a day, compared to none in the controls. Smoking was significantly associated with having TB among HIV negative hospitalized patients (OR 4.5, $P = 0.009$). 47% (35/74) of the TB cases consumed alcohol and there was a strong association between smoking and alcohol consumption across both groups (OR 9.0, $P = 0.000$).

Conclusions: There is a higher prevalence of smoking among TB patients than other hospitalized patients. The association between TB and smoking is significant among those without HIV. Prevention and cessation of smoking should be integrated into TB control initiatives in Karasburg district. There is need for more studies to determine the association between smoking and TB in other areas of Namibia.

SOA-530-27 The association of household air pollution and tuberculosis in women and children in Pune, India

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Background: Household air pollution (HAP) from cooking fuels and secondhand tobacco smoke (SHS) is a known risk factor for respiratory disease, however HAP has yet to be definitively associated with tuberculosis (TB). In India, an estimated 74% of households are exposed to HAP. We assessed the association of exposure to HAP and TB in women and children in Pune, India.

Methods: A matched case-control study was conducted among adult women and child index TB patients and healthy controls matched on geography, age, and sex. Exposure to HAP was assessed using structured questionnaires for cooking fuels and other HAP sources, such as secondhand tobacco smoke, and measured concentrations of particulate matter less than 2.5 microns (PM_{2.5}) were collected for a period of 24 hours in each household. HAP exposure was compared across cases and controls using conditional logistic regression.

Results: A total of 118 individuals in 59 matched pairs were enrolled into the study, including 32 pediatric index cases and their matched controls, and 27 adult index cases and their matched controls. High levels of exposure to PM_{2.5} were found across all homes (median 24-hour time-weighted average of 184 µg/m³; IQR: 107–345), and exposure metrics for high HAP tended to be associated with TB. The use of kerosene was significantly associated with TB (OR 11.18; 95%CI 1.24–100.8) in adjusted analysis. Households with the greatest number of hours of PM_{2.5} above 75 µg/m³ had a substantial increase in odds of TB (OR 3.30; 95%CI 0.95–11.51), and a dose-response effect was seen with increasing quartile (OR 1.72; 95%CI 0.94–3.15), with both of these measures approaching statistical significance.

Conclusions: Measures of higher HAP tended to be associated with TB in adjusted analysis, providing evidence that women and children exposed to high levels of HAP may be at greater risk for TB. Across all study homes, participants were exposed to extremely high levels of PM_{2.5}. Interventions reducing HAP are needed in this population burdened both by high exposure to HAP and a high incidence of TB.

SOA-531-27 Interaction between smoking and preexisting tuberculosis on lung cancer

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Background: Both smoking and preexisting tuberculosis (TB) are frequently considered as causes of lung cancer.

However, relatively little attention was paid to the interaction between smoking and prior TB history on lung cancer, even though studies adjusted for each other in the models. The study aims to identify additive and multiplicative interaction between smoking history and preexisting TB on lung cancer

Methods: Data was extracted from a National Health Insurance Service (NHIS) sample cohort dataset including about 1 million people from 2002 to 2013. About 10% of them participated in the regular health examination (rHE) that includes smoking and previous TB history. Among participants of rHE in 2002, persons who have no lung cancer (C34.X) in 2002 were included in the study. They were followed up until 2013 and identified to be diagnosed as lung cancer during the follow-up period. A multivariate and stratified logistic regression models were constructed to analyze the impact of smoking and prior TB on lung cancer, after adjusting for potential confounders (age, sex, income, body mass index, drinking and exercise). In addition, relative excess risk due to interaction (RERI) was used as an additive scale and multiplicative interaction was measured.

Results: In total, 83 043 participants were included from the NHIS dataset. Among them, 1963 participants had preexisting TB history and 30 875 participants categorized as ex- or current smokers. Compared with no TB history/never smoked group, no TB history/ever smoked, prior TB/never smoked group, and prior TB/ever smoked group were increased the risk to be diagnosed as lung cancer during the follow-up period and odds ratios were 1.59 (95%CI 1.39–1.81), 1.49 (95%CI 1.02–2.17) and 1.69 (95%CI 1.13–2.54), respectively. As an additive scale of interaction, RERI was –0.38 (95%CI –1.26–0.49, *P* = 0.392). Multiplicative scale was 0.72 (95%CI 0.41–1.24, *P* = 0.234)

Conclusions: Smoking and preexisting TB would be considered as risk factors of lung cancer. However, there was a negative interaction between smoking and TB on lung cancer. Further biologic study would be required to explain the negative interaction between both risk factors on lung cancer.

SOA-532-27 Tobacco cessation intervention of civil society (Seva Sadhan) plays a vital role in treatment adherence among tobacco-using TB patients

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Background: Both TB and tobacco are major global public health concerns, causing millions of deaths each year. Active consumption of tobacco/smoking increases the risk of tuberculosis (TB) infection two times and is significantly associated with recurrent TB and TB

mortality. Observational studies have shown associations between tobacco/smoking and poor TB treatment outcomes such as increased loss to follow-up rate, severity of disease, drug resistance and slow smear conversion.

Objectives: To quantify the effects of civil society organisation tobacco smoking cessation programme intervention on the treatment outcomes of people with Pulmonary TB in Muddebihal TU, Bijapur District Karnataka.

Methods: In Bijapur District, there are 6 tuberculosis units, out of which Muddebihal TU has been reporting with high default rate, death rate and failure rate. The Civil society organisation (SS) with help of RNTCP team mapped the Muddebihal TU on going DOT patients. With the help of NTCP support, Seva sadhan volunteers applied Tobacco cessation intervention to TB patients. The intervention focuses patient centric approach with periodic weekly counselling sessions to patient and family on Tobacco and its causation factors for ill health using audio-visual aids provided by NTCP and also taught them ill effects of tobacco affects the treatment of TB.

Results: Before intervention, in 2014, out of 375 patients 274 TB patients are tobacco consumers. Default rate of these tobacco consuming patients is 13.1%, failure rate is 3% and death rate is 8.5%. In 2015, of 295 TB patients, 218 patients are tobacco consumers. After the Civil society organisation (SS) tobacco cessation intervention, default rate of the tobacco-consuming patients is 7.1%, failure rate is 1% and the death rate is 6.8%.

Conclusions: Tobacco cessation intervention in TB patients is found to be more effective in reducing defaults and this may be replicated in all TB units of India.

SOA-533-27 Attitudes about the impact of smoking and smoking cessation on TB among health care workers at TB facilities in Georgia

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Background: Smoking is a risk factor for developing active tuberculosis (TB), and it increases the risk of poor treatment outcomes among patients with TB. Given limited available data, we aimed to determine attitudes of healthcare workers (HCWs) at TB facilities regarding the impact of tobacco use and tobacco cessation on TB treatment.

Methods: We conducted a cross-sectional survey in the country of Georgia from May–December 2014. Eligible participants included adults (≥ 18 years) HCWs at Georgia National TB facilities. Participants completed a 20-minute anonymous survey about self-reported

tobacco use and attitudes of smoking cessation. Logistic regression was used to estimate the association between current smoking and attitudes regarding the impact of smoking on TB treatment outcome.

Results: A total of 431 HCWs who worked at the National TB Program participated; 87.5% of HCWs were female and HCW median age was 50 years (range 20–77). Overall, 13.7% of HCWs indicated they were current smokers; male HCWs had significantly higher rates of smoking than female HCWs (46.3% vs. 9.0%). Among physicians and nurses ($n = 255$), most ($n = 169$, 66.3%) were aware of nicotine replacement therapies but only 67 (26.3%) had received training on cessation approaches with patients. Among physicians ($n = 86$), 12.9% reported discussing cessation with smoking patients only during the first TB patient visit. Most physicians ($n = 46$, 53.5%) had been asked by patients about electronic-cigarettes and 26 (30.6%) reported not knowing enough to make a recommendation. Of all HCWs, 115 (26.7%) reported that they did not believe smoking impacts TB treatment outcomes. In multivariable analysis, physicians who smoked were significantly more likely to report that smoking does not impact TB treatment compared to non-smoking physicians (aOR 3.8, 95%CI 1.2–2.5).

Conclusions: Smoking rates were high among male HCWs and few physicians or nurses received training on smoking cessation approaches for patients with TB. More than a quarter of HCW did not believe that smoking impacts TB treatment outcomes, and this belief was especially pronounced among physicians who smoked. Training HCWs about available smoking cessation programs for TB patients may enhance smoking cessation efforts of patients with TB and improve TB treatment outcomes.

SOA-534-27 Pulmonary tuberculosis and its association with tobacco smoking habits in Panniya tribes of India

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Background: The tribal populations throughout India have remained socially and culturally alienated from mainstream Indian society until developmental and conservation activities in tribal areas forced interactions between them. Pulmonary tuberculosis is a major public health problem among Panniya tribes, a marginalized tribal group in Kerala state, South India. Previous studies have documented a high prevalence of tobacco use among Panniya Tribes in Nilgiri District. However, little is known about their correlation exists between tobacco habit and pulmonary tuberculosis. The aim of this study was to evaluate the Pulmonary Tuberculosis among non smoking and smoking tobacco Panniya tribes.

Methods: A cross-sectional study was conducted in two tribal villages Wayanad district of Kerala state. The survey was done among 688 nonsmoking and 483

smoking Panniya tribal populations from January 2014 to June 2014 after approval from the Institutional ethical committee. Information on smoking status, type of tobacco smoked, quantity of tobacco smoked and duration of tobacco smoking was collected from cases and controls using a questionnaire.

Results: In this study pulmonary tuberculosis was found to be far more prevalent among smoking Panniya tribes than among the non smoking Panniya tribes. ($P < 0.0001$). The prevalence of pulmonary tuberculosis was found to be 8% amongst smokers. This was much higher than the 0% found among the non smokers. The prevalence respiratory disease was found to be 41% amongst smokers and 3% found among the non smokers. Among the tobacco smokers a statistically significant relationship was observed between pulmonary tuberculosis and poor access to health care ($P < 0.001$).

Conclusions: The present study demonstrates gross disparities in pulmonary tuberculosis among smoking and non-smoking Panniya tribes. There is an urgent need to develop and implement culturally appropriate awareness raising activities to target tobacco habit to support the efforts to control pulmonary tuberculosis in this community.

SOA-535-27 Barrier identification to smoking cessation for drug-resistant tuberculosis patients in South Africa

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Background: In South Africa, drug resistant tuberculosis (DR-TB) remains a significant cause of morbidity and mortality. The association between the long-term health effects of smoking and the risk of adverse TB outcomes among DR-TB patients, including increased periods of infectiousness has been reported in South Africa and other high burden DR-TB countries. This paper reports on a study that aimed to determine barriers to smoking cessation among DR-TB in-patients at King DiniZulu Hospital in the city of Durban, South Africa.

Methods: A qualitative design that included in-depth interviews with a purposive sample of DR-TB inpatients was employed to assess barriers to smoking cessation. The sample included in-patients who self-identified as smokers (aged 18–60 years, 15 males and 5 females). Open-ended questions were utilized to establish patients' current smoking behavior, knowledge of health risks, interest in quitting, and preferences for cessation support. Interviews were recorded with patient permission. In order to generate themes around barriers to cessation, interview recordings were transcribed and entered into QSR NVivo10 qualitative software.

Results: Generally the patients were interested in smoking cessation and conveyed frustration at the lack of appropriate support. The majority of patients were unaware of any available smoking cessation interventions. Nearly all patients identified cravings as a barrier

to cessation, which were often linked to long term smoking behaviour. Over half of patients described smoking as a coping mechanism during their admission. In order to reduce the time spent on smoking, some patients indicated the need for extra-mural activities. Availability of cigarettes within the hospital environment also deterred cessation. Most patients indicated the desire for an intervention that will practically assist them with smoking cessation aids.

Conclusions: These findings indicate the need for a missed opportunity of a holistic smoking cessation intervention as an integral component of DR-TB management in South Africa. Many patients expressed an interest in nicotine replacement therapies as well as psychological support to cessation. Additionally, offering extra-mural activities and reducing the availability of cigarettes in TB facilities may reduce cravings and the number of cigarettes consumed.

SOA-536-27 Quantifying the potential impact of smoking cessation campaigns on tuberculosis in Indonesia

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Background: Cohort and case control studies have shown prolonged smoking to be significantly associated with a higher risk for development of active tuberculosis (TB). Though such studies quantify the individual risks of smoking, they do not account for the cumulative population level effects resulting from onward transmission. We focus on Indonesia where the prevalence of smoking among adult males is nearly 70% and TB prevalence is approximately 600 per 100 000 adults. Employing mechanistic mathematical models of TB transmission which are consistent with observed individual risk, we estimate the impact of smoking on population level TB morbidity and mortality. We then quantify the impact that smoking cessation campaigns could have on the future of the TB epidemic between 2016 and 2025.

Methods: We construct an individual based, dynamic mathematical model of TB transmission in Indonesia. The model accurately reflects the overall age demographics of the country and is calibrated to both age specific TB prevalence estimates from the 2015 national prevalence survey and age specific TB mortality estimates. Individual level relative risk of active TB development is parameterized in terms of cumulative smoking duration according to published estimates from cohort and case control studies.

Results: The mathematical model was able to reproduce observed patterns of both temporal and age-stratified TB prevalence and mortality. We found that the rate and degree to which smoking cessation campaigns could reduce TB burden depends strongly upon the relative importance of recent TB transmission vs. endogenous reactivation in the epidemiological setting. If the epidemic is dominated by recent transmission cessation campaigns result in more substantial and rapid impact.

Conclusions: In high TB burden countries with high prevalence of smoking, tobacco control strategies have the potential to significantly reduce TB morbidity and mortality. Estimates of the potential magnitude of impact will depend on understanding the relative contributions of recent transmission and endogenous reactivation to TB incidence.

SOA-537-27 Seasonality of tuberculosis in Israel and serum 25-hydroxyvitamin D correlation, 2001–2011

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Background: Several studies have suggested that the incidence of tuberculosis varies with season. This study aimed to determine the seasonality of tuberculosis in Israel and to explore possible associations with climatic variables and average serum 25-hydroxyvitamin D levels, as well as to analyze the trends amongst different sub-populations, including migrants.

Methods: All laboratory-confirmed tuberculosis cases reported between 2001 and 2012 in individuals resident in Israel for at least one year before diagnosis were included. Climatic variables included average temperature and average ultraviolet radiation. Additionally, mean serum level of 25-hydroxyvitamin D of 25% of all the Israeli population was recorded during the study-period.

Seasonal trends were analyzed by dividing all cases diagnosed each year into four quarters according to climatic logic. Newly diagnosed tuberculosis cases in each seasonal quarter were calculated as a proportion of the total study period, thus yielding the mean proportion. Seasonality was defined as case proportion amplitude (CPA) >5% between the season of peak and nadir incidence.

Results: A total of 4,936 tuberculosis cases reported in Israel during the 12 years of the study period, 2895 (58.6%) had laboratory confirmation and lived in Israel >1 year.

The overall incidence peaked during the winter and spring months and lower in the summer and fall, with a CPA of 5.0% between the spring peak and the fall nadir ($P = 0.025$). This trend was prominent among patients living in the southern latitudinal area ($n = 587$), migrants born in Africa ($n = 754$) and those diagnosed with extra-pulmonary tuberculosis ($n = 486$). Serum 25-hydroxyvitamin D levels were high during summer/fall and lower in winter/spring. The seasonal pattern of 25-hydroxyvitamin D mirrored that of tuberculosis, peaking oppositely in the summer/fall and nadir in the winter/spring, but in a similar differences between the peak and nadir (18.7% and 19.8%, $P = 0.047$ and $P = 0.002$, respectively), Pearson correlation coefficient was 0.40 ($P = 0.005$).

Conclusions: Tuberculosis exhibited a seasonal tendency in Israel, with the spring-peak and fall-nadir pattern,

while serum vitamin-D serum level showed the opposite trends and was higher in fall and lower in the spring. Seasonality trends were more significant among migrants from Africa and those diagnosed with extra-pulmonary tuberculosis.

SOA-538-27 The proportion of deaths from tuberculosis, tuberculosis with diabetes and tuberculosis with cigarette consumption at age 15 years and above

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Background: Tuberculosis is an infectious disease that is still the focus of attention in Indonesia, due to the high morbidity and mortality in the last decade. Results of 2007 Basic Health Research showed the proportion of TB deaths by 7.5%, which was ranked second cause of death after Stroke. Results of National Tuberculosis Prevalence Survey 2013–2014 showed the rate of 759 per 100 000 population aged 15 years and above with bacteriological confirmation. Data from the WHO Global Tuberculosis Report 2015 shows that India, Indonesia and China had the largest number of cases: 23%, 10% and 10% of the global total. The purpose of this study is to provide an overview of the proportion of deaths from TB, TB with DM and TB with the consumption of cigarettes at age 15 years and above, found in 2014 Sample Registration System.

Methods: All mortality cases in SRS (including death events at hospital) were collected by trained paramedical personnel through household visits, using verbal autopsy instruments (paper & pencil) and the diagnosis were verified by trained physicians based on International Statistical Classification of Diseases and Related Health Problems (Tenth Revision), grouped by Special Tabulation List For Mortality (selected list).

Results: The Indonesia Sample Registration System (SRS) 2014, covers 128 subdistricts in 119 districts or cities (30 provinces). The population covered was about 3.5% of the total national population. According to the Indonesia SRS, the proportion of Tuberculosis deaths of 5.7% was ranked the fourth cause of death after Cerebrovascular Disease (I60–I69), Ischaemic Heart Disease (I20–I25), and Diabetes with complications (E10–E14). The number of Tuberculosis deaths accompanied by Diabetes was 8.1%, and 55.9% were active tobacco smokers. While all deaths due to diabetes, which were accompanied by Tuberculosis was 3.6%.

Conclusion: The proportion of deaths due to Tuberculosis with Diabetes is quite high and more than half the of the deaths from tuberculosis consumed tobacco.

POSTER DISCUSSION SESSIONS

01. An intimate relationship: drug resistance and genes

PD-600-27 Molecular and phenotypic diagnosis of ethionamide resistance in *Mycobacterium tuberculosis*: a seven-year experience in France

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Background: Ethionamide (ETH) is a drug used to treat multidrug-resistant tuberculosis (MDR-TB). However, diagnosing ETH resistance (ETH-R) is still challenging. ETH-R has mainly be related to mutation of EthA (mono-oxygenase activating ETH), EthR (regulates EthA), InhA (targeted by the activated drug, involved in cell wall biosynthesis) and InhA promoter.

Methods: We reviewed the strategy used for detecting ETH's resistance at the French National Reference Center for Mycobacteria among 527 isolates received from 2008 to 2014. Genotypic ETH's resistance detection was performed by sequencing *ethA*, *ethR*, *ethA-ethR* intergenic region, *inhA* and its promoter; whereas the phenotypic ETH's susceptibility testing (PST) was performed by the reference proportion method.

Results: Among the 371 ETH-R isolates, mutations were found in 68% of the strains ($n = 251$); mainly in *ethA* (48%) or in the *inhA* promoter (38%). Among the 131 ETH-susceptible isolates, 73% harbored no mutation ($n = 96$), whereas 27% harbored at least one mutation (29 in *ethA*, 4 in the *inhA* promoter, 2 in *ethR*). We analyzed separately the 25 ETH-susceptible isolates displaying an abnormal proportion of resistant mutants (i.e.; $>1\%$ but $<10\%$ resistant mutants): 32% harbored no mutation ($n = 8$), whereas 78% harbored at least one mutation (13 in *ethA*, 4 in the *inhA* promoter, 1 in the intergenic region *ethA-ethR*).

Conclusions: Altogether, the performances of our genotypic strategy to diagnose ETH-R has improvable sensitivity (68%) and specificity (73%). These results, as well as the high number of strains with a difficult to interpret PST (5%), highlight the need of improving both genotypic and phenotypic ETH susceptibility testing methods.

PD-601-27 Lack of association between genotypic polymorphisms in *ubiA* and ethambutol resistance in clinical isolates of *Mycobacterium tuberculosis* in North India

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Background: Drug resistance is a major setback to efficient treatment of tuberculosis (TB). Spontaneous mutations are a prominent reason for development of resistance against first line TB drugs. Diagnostic assays to detect drug resistant TB, rely on definite genotypic indicators/mutations. However definite genetic markers are unavailable for resistance to ethambutol (EMB). Studies from across the world have focused on the gene *embB*, involved in polymerization of cell wall arabinogalactan. Mutations at codon 306 (Met to Val/Ile) have been reported in 40-60% EMB resistant clinical isolates. Recently the presence of mutations in *Rv3806c* (*ubiA*) in clinical isolates resistant to EMB have been reported. The present study was performed to find a possible association between *ubiA* mutations and EMB resistance in clinical isolates of *M. tuberculosis* from North India.

Methods: 220 clinical isolates of *M. tuberculosis* were tested for susceptibility to EMB, of which 24 were EMB resistant while 24 EMB susceptible isolates were taken as control. The entire gene *ubiA* as well as mutational hotspot region of the gene *embB*, and upstream region of *embA* were screened for polymorphisms. The results of mutation analysis were also correlated with the minimum inhibitory concentration (MIC) of EMB for each isolate.

Results: A polymorphism at codon 149 (GAA to GAC) was the most common in *ubiA* occurring in 25% (6/24) resistant strains and 25% (6/24) sensitive strains. No other mutation significantly associated with resistance was observed at *ubiA*. Mutation (ATG to ATC/GTG) at codon 306 of *embB* was observed in 58.3% (14/24) resistant isolates and in none of the sensitive isolates. A mutation, C to A, at -11 (upstream region) of *embA* was found in 12.5% (3/24) resistant strains but always in conjunction with *embB306* mutation, associated with a higher level of resistance (MIC $>16\mu\text{g/ml}$) than with mutations at *embB306* alone.

Conclusions: This preliminary investigation showed that the polymorphisms found in *ubiA* were not significantly higher in EMB resistant clinical isolates of *M. tuberculosis* from North India to indicate their involvement in ethambutol resistance in Indian isolates. However, an extended study on a higher number of clinical isolates of *M. tuberculosis* is needed to further validate this observation.

PD-602-27 Persistence of highly drug-resistant Beijing strain in the Eastern Cape region of South Africa

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Background: Drug resistance is a serious problem in South Africa, with most cases detected in KwaZulu-Natal, Western Cape, and Eastern Cape Provinces. Statistics showed that a 2.2 fold increase in number of MDR-TB cases in Eastern Cape region in 2009. In addition the virtually untreatable strain known as atypical Beijing was reported from Eastern Cape in 2013, accounting for approximately 90% of pre-XDR and XDR cases. Although the reason for this dramatic increase in drug resistant TB cases is not understood, transmission could be the driving cause of the epidemic. **Objective:** the aim of this study was to assess the clonal transmission of drug resistant strains in a high burden district of Eastern Cape province.

Method: A total of 177 prospective RIF resistant specimens collected from Xpert Rifampicin Resistant cases in the NMM district of Eastern Cape. These isolates were collected between January 2015 to January 2016 as part of the laboratory-based surveillance programme conducted at Centre for Tuberculosis. Drug susceptibility testing was performed using MGIT 960 and MTB-DR_{plus} line probe assay. All isolates were genotyped using spoligotyping and 24-loci MIRU-VNTR typing.

Results: Eighty six (53%) of the 177 isolates were confirmed MDR-TB strains. Spoligotyping identified 16 families with Beijing being the most predominant family, comprising 94/177 (53%). Among the Beijing isolates, 25 (26.6%) had identical spoliotyping and MIRU-VNTR typing pattern. Analysis of the Line probe assay of the clustered Beijing isolates showed the presence of the rare mutation in *inhA*, as well as the *KatG* and *rpoB* gene, markers indicative of the atypical Beijing strain.

Discussion: The genotyping data from the study suggests drug resistant Beijing strain is being clonally transmitted in the region, as demonstrated by the cluster with characteristics of atypical Beijing genotype. The same clone has also been identified from previously characterized group of patients ($n=23$) failing XDR-TB treatment in the Eastern Cape Province.

Conclusion: The study has shown that the highly resistant Beijing clone continues to be transmitted in the Eastern Cape region, emphasizing need for improved control measures by careful monitoring of trends, transmission routes of this strain, and the provision of effective therapy.

PD-603-27 Insights into the application of whole genome shotgun sequencing of *M. tuberculosis* in the highly endemic region of Mumbai, India

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Background: Whole genome shotgun sequencing (WGS) of *M. tuberculosis*, has revived the hope to study rapid accumulation and transmission of drug resistance, which is global threat to public health and is a major concern in the Indian context.

Methods: We performed WGS of 69 *M. tuberculosis* clinical isolates from Mumbai using Illumina 2X150 paired end sequencing. WGS based genotyping and resistotyping was ascertained using the Mykrobe predictor software. Phenotypic drug susceptibility testing (DST) was done using BACTEC MGIT 960 SIRE kit and/or Buddemeyer method.

Results: WGS based resistance calling identified 84% of the MDR strains and 74% of the drug susceptible strains. Crucially WGS also predicted 15 Pre-XDR and 1 XDR isolates. Accuracy of prediction of resistance of the isolates to isoniazid was 80% (28/35), rifampicin was 75% (24/32), ethambutol was 45% (9/20) and streptomycin was 79% (19/24). Phylogenetic analysis detected a clonal group consisting of 3 drug susceptible isolates. A small sample size limited further phylogenetic analysis.

Conclusions: The study demonstrated the application of WGS technology for molecular epidemiological insights into evolution and transmission of drug resistance and as a useful tool for simultaneous detection of MDR, XDR and XXDR. The genotypic mutation panel of Mykrobe predictor which currently includes the HAINS panel, can be further verified and expanded using mutations verified in large WGS studies. Improved databases will further improve sensitivity of analytic methods of molecular drug resistance, with shorter turn-around time of hours as compared to weeks with conventional microbiological DST. WGS of larger sample sizes may provide insights into the retrospective and real-time monitoring of evolution of drug resistance in the highly endemic locale of Mumbai. In such a study a phylogeny indicated by a large number of unlinked MDR isolates may indicate evolution of drug resistance due to improper therapy. Conversely, phylogenetically linked MDR isolates may indicate transmission of MDR in the community. Finally in conjunction with powerful simulation techniques and geographical modelling, WGS provides unparalleled disease surveillance for formulating local, national and international policies to counter the growing threat of drug resistant tuberculosis.

PD-604-27 Pattern of *rpoB* gene mutations in *Mycobacterium tuberculosis* isolates of pulmonary TB patients using Xpert® MTB/RIF in Ethiopia

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Background: GeneXpert assay utilizes five differently colored molecular beacons that bind to a different target segment within the *rpoB* core region. Over 95% of rifampicin resistance cases are associated with mutations that occur within an 81-bp region of the *rpoB* gene corresponding to 507-533 codons that encodes 27 amino acids in the subunit of RNA polymerase of *Mycobacterium tuberculosis*. It is termed rifampicin resistance determining region (RRDR). We present the pattern of *rpoB* mutations in the clinical isolates of rifampicin resistant *M. tuberculosis*.

Methods: GeneXpert testing services are provided in 49 laboratories in the two regions. A total of 7458 sputum samples from presumptive MDR-TB cases were tested by GeneXpert during 1 October 2014–30 September 2015. Data on the pattern of *rpoB* mutation were collected from GeneXpert software database.

Results: Of 7458 samples processed, 286 (3.8%) rifampicin resistant *M. tuberculosis* were detected. The resistance was conferred by all five (A-E) *rpoB* gene probe mutations in the 81 bp-RRDR hotspot regions of *M. tuberculosis*. Mutation was observed predominantly at probe E, D and B: 65.0%, 18.2%, 9.1%, respectively. There was only one case of mutation in probe A in Oromia Region. A rifampicin resistance associated with more than one probe mutation was also detected and probes B and D accounted for 3.5%. There was no regional variation in the pattern of *rpoB* mutations ($P = 0.19$) (Table).

Conclusion: Most frequent mutation was observed at the commonest probe E, B & D, similar to findings elsewhere; however our data also demonstrated uncommon mutations including probe C and multiples combination of probes. Such information on *M. tuberculosis* *rpoB* type of mutation prevailing in a defined area could help to devise better policies and practices for effective control of MDR-TB.

Table *rpoB* gene mutation profile in RR TB cases

Mutant probes	Amhara	Oromia	Total mutant probes observed	X ² (P value)
B	7(5.5%)	19(12%)	26	6.194 (0.185)
C	4(3.1%)	3(1.9%)	7	
D	20(15.6%)	32(20.3%)	52	
E	89(69.5%)	97(61.4%)	186	

PD-605-27 Detection of isoniazid and rifampicin resistance in clinical *Mycobacterium tuberculosis* isolates from Pakistan using the GenoType® MTB-DRplus assay

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Background: GenoType MTB-DRplus is a molecular assay for detection of *Mycobacterium tuberculosis* resistance to isoniazid (INH) and rifampicin (RMP). Identification of INH resistance is based on occurrence of mutations in the *katG* gene while for RMP resistance, mutations in the *rpoB* gene are investigated.

The aim of this study was to evaluate the ability of the assay to detect INH and RMP resistance among strains of *M. tuberculosis*, isolated from Pakistani TB patients.

Methods: 100 MDR *M. tuberculosis* strains were isolated between January and September 2014. DST was performed using 1% proportion method with INH and RMP critical concentrations of 0.2 µg/ml and 40 mg/l, respectively. Genomic DNA was extracted by CTAB method. The GenoType MTB-DRplus assay (Hain Life-science, Germany) was performed following the manufacturer's instructions.

Results: In the *katG* gene, 16% strains carry mutations in G944C transition, conferring Ser315Thr amino acid change. 34% strains did not carry the *katG* mutation. Mutations in the *mabA-inhA* promoter region were detected in 29% strains (C-15T - in 10 strains, and T-8C - in 2 strains). Seventy-seven (77%) strains tested harbored a mutation in *rpoB* gene. Mutations in the *rpoB* gene were of four types: C1349T, A1304T, C1333G, and TC1324CA found in 63 (63%), 11 (11%), 8 (8%), and one (1%) strain, respectively. Of the 100 strains designated as MDR, GenoType MTB-DRplus confirmed this phenotype in only 62 strains. The results of GenoType MTB-DRplus and the conventional drug susceptibility method were consistent in 70% (70/100) for INH, and 77% (77/100) for RMP.

Conclusions: As evidenced in this study, the major concern with the GenoType MTB-DRplus assay were false negative results. In comparison to conventional DST, the assay was unable to detect 30 (30/100; 30%) strains resistant to INH and 23 (23/100; 23%) strains resistant to RMP. The GenoType MTB-DRplus failed to identify 38 MDR (38/100; 38%) strains. Resistance in those strains probably originate from mutations in other codons and/or genes than those covered by test. For detecting INH and RMP resistance in TB cases, especially in high TB incidence countries, such as Pakistan, molecular approaches should still be a complement rather than a replacement to conventional DST.

PD-606-27 Detection of multidrug resistance and characterization of mutations in *Mycobacterium tuberculosis* isolates, IRL Dharampur, Himachal Pradesh, India

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Background: Multidrug-resistant strains of *Mycobacterium tuberculosis* threaten tuberculosis control and prevention efforts. We undertook this study to detect multi-drug resistant tuberculosis (MDR-TB) among MDR-TB suspects, and common mutations among MDR-TB cases using GenoType MTB-DR^{plus}.

Methods: Sputum samples of MDR suspect received were subjected to smear microscopy. Smear negative for AFB were inoculated on solid culture (H₇) medium. The AFB positive smears and cultures were processed using line probe assay to detect common mutations in the *rpoB* gene for rifampicin and *katG* and *inhA* genes for isoniazid. Data was analysed using Epi info 7.1.3, 2013.

Results: Of the 1706 presumptive MDR patients, tested on line probe assay 117 (10.43%) were multi-drug resistant. Mono rifampicin and isoniazid resistant was observed among 35 (3.12%) and 114 (10.16%) samples respectively. There were 69/117 (58.97%) males. The majority 79/117 (67.52%) were in the age group of 15–45 years with more females 41(51.90%) in this age group. Missing WT8 along with mutation in codon S531L was the commonest pattern for rifampicin resistant isolates (54.6%). Missing wild type (103/117; 88%) along with mutations in codon S315T1 of the *katG* gene was commonest pattern for isoniazid resistant isolates (98.91%). *InhA* mutations were found in 8/117 (6.83%) of isoniazid resistant strains which were all of C15T type. Mixed pattern to rifampicin with all wild type probes present along with presence of one or more mutant bands was found in 16 /152 (10.52%), commonest being S531L (6/16; 37.50%).

Conclusions: The common mutations obtained for rifampicin and isoniazid in the study were mostly similar to those reported earlier. However higher mono isoniazid resistant may threaten the success of ongoing TB control programme. There is a need for early drug susceptibility testing, and initiation of appropriate treatment along with continued surveillance for MDR-TB among newly diagnosed TB cases.

PD-607-27 Evaluating next generation sequencing pipelines for *Mycobacterium tuberculosis* complex genome reconstruction

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Background: With significant reductions in sequencing cost, a growing number of commercial sequencing

facilities and increased availability of personal bench top sequencers, the potential of WGS to improve TB surveillance and control has been shown. Despite this, the current bottleneck of WGS is storage, analysis and interpretation of data generated to improve public health and patient care. Data analysis requires bioinformatics capacity, high computing and data storage infrastructure, which are major challenges in Africa. To determine how analysis of WGS data can be carried out in a typical African setting without computing centres or clusters to provide meaningful biological information, we performed a comparative analysis of pipelines for *M. tuberculosis* complex genome reconstruction.

Methods: WHO-TDR together with the Institute of Tropical Medicine established a strain bank to support research on drug resistance mechanisms. Samples underwent target gene sequencing and membrane based spoligotyping as gold standards. WGS of strains was carried out. We compared command-line based pipelines using shell scripts and web-based tools for analyzing *M. tuberculosis* WGS. We assessed analysis runtime and space used for data storage and compared pipelines for robustness in accurately detecting mutations found by target gene sequencing, in *rpoB*, *KatG*, *inhA*, *rpsL* and *embB*. We also compared concordance between in-silico predicted and membrane based spoligotypes.

Results: Six Linux-based pipelines have been compared using sequencing results of 12 strains. Fastq files of 500 megabytes - 2 gigabytes (GB) were analyzed. For the 12 strains, wall clock time for processing files on the command-line ranged from 2478–69 689 seconds and disk space used from 20–71 GB. Pipelines differed in complexity and number of software dependencies required to run analysis. However, all pipelines accurately detected the mutations found by target gene sequencing and additional nucleotide polymorphisms.

Conclusions: Despite excellent concordance between pipelines in detecting resistance mutations in genomes that were confirmed by target gene sequencing, file processing time and disk space usage differed significantly. In settings with limited data storage infrastructure, pipelines requiring minimum space will be advantageous. For diagnostic utility, pipelines with shorter execution time will be advantageous.

PD-608-27 Resistance-conferring mutations with fitness cost among HIV-positive individuals from Uganda

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Background: MDR-TB is considered to be less transmissible, due to fitness cost associated with drug resistance-conferring mutations in essential genes. We hypothesised that TB drug resistant-conferring mutations with fitness cost are more frequent among HIV-positive compared to HIV-negative patients, given their greater susceptibility for infection.

Methods: We analysed all strains from two TB drug resistance surveys conducted in Uganda between 2008 and 2011. Strains phenotypically susceptible to rifampicin and/or isoniazid were assumed wild type, otherwise, we performed whole-genome sequencing. *rpoB*531 and *katG*315 mutations were considered without fitness loss whereas other *rpoB* codons and non-*katG* were considered with fitness loss.

Results: Of the 897 TB patients, 591 (63.1%) were male, 286 (32.1%) were HIV-positive and 93 (10.3%) were previously treated for TB. Resistance conferring-mutations to rifampicin were found in 8 genomes (0.9%) at *rpoB*531 and 7 (0.8%) at other *rpoB* codons, whereas for isoniazid, 26 (2.9%) had *katG*315 mutation and 7 (0.8%) mutations in *fabG*1. Two patients had compensatory mutations in the *rpoC* codon (N698S and V483A) in addition to *rpoB*531. Mutations with fitness loss in HIV-positive and HIV-negative patients, respectively: Non-531 *rpoB*: 1.03% ($n = 3$), 0.71% ($n = 4$); OR: 2.2 (95% confidence interval [CI] 0.83–5.77), *fabG*1: 0.40% ($n = 1$), 1.0% ($n = 6$); OR: 0.40 (95%CI 0.07–2.20). Mutations without fitness loss in HIV-positive and HIV-negative patients, respectively: *rpoB*531: 1.49% ($n = 4$), 0.69% ($n = 4$); OR: 1.46 (95%CI 0.58–3.68), *katG*315: 3.86% ($n = 11$), 2.55% ($n = 15$); OR: 1.54 (95%CI 0.81–2.90). The effect of HIV on the presence of mutations differed for patients in Kampala compared to those outside Kampala, with no *rpoB*531 mutations detected among HIV-positive individuals, a reduced HIV effect for *katG*315, and an increased effect of HIV for *fabG*1. HIV-positive individuals at the national referral hospital TB ward had a high risk of having non-531 *rpoB* mutations (OR 8.39; $P = 0.021$ 95%CI 1.39–50.64).

Conclusions: Our data do not support the hypothesis that resistance mutations with fitness cost are more often present in HIV-positive individuals. The higher risk of reduced-fitness *rpoB* mutations with hospitalization suggests a role for nosocomial transmission.

PD-609-27 Performance of spoligotyping applied directly on sputum for genotypic characterization of *Mycobacterium tuberculosis* complex

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Background: This study aimed to determine the performance of direct spoligotyping (on sputum) relative to its yield on culture, for genotypic characterization of *Mycobacterium tuberculosis* complex, to lessen potential culture bias against difficult growers.

Methods: Smear-positive sputum from new tuberculosis patients diagnosed in Cotonou, (Benin) were included. After decontamination using the Petroff method, an aliquot of decontaminated sputum was cultured on Löwenstein Jensen medium (90 days), and another aliquot was used for direct spoligotyping. DNA was extracted by heat-inactivation for isolates, and by the Maxwell®16 Tissue DNA purification kit for decontaminated sputum. Spoligotyping was done according to the standard method for all samples, and obtained patterns from sputum were compared vs. their derived culture isolates, considered as gold standard.

Results: From 100 patient's sputum, 77 (77%) yielded a positive culture. Spoligotyping result was available for 76 (98.7%) culture-positive sputum, and for 22 (95.65%) of the 23 sputum with negative or contaminated culture. In total spoligotype pattern was available for 98 (98%) direct sputum extracts. There was a good 93.42% (71/76) agreement between sputum- and isolate-derived profiles. For 3 of the 5 discrepancies, the interpretation of spoligotype patterns yielded the same lineage and the same family, with respectively 2, 9 discrepant spacers (false negative in sputum), and 3 discrepant spacers (false positive in sputum); while for the 2 remaining discrepancies (respectively 8 and 32 discrepant spacers), different lineages were obtained, including a likely instance of mixed infection. The comparison of lineage variation among culture-negative vs. -positive specimens showed 54.6% of strains from ancestral lineages (*Mycobacterium africanum* West African 1 and 2, Indo-oceanic) among culture-negative specimens vs. 29.9% among culture-positive specimens, with a statistically significant 24.7% increase (95%CI 1.5%–47.9%, $P = 0.030$) of such strains among culture-negative specimens, unlike modern lineages.

Conclusions: Direct spoligotyping on sputum is effective, and saves time and effort. It has an important advantage to determine spoligotype patterns in sputum that may not yield a positive culture, allowing a more precise unbiased determination of the population structure of the *Mycobacterium tuberculosis* complex. Differences in culture isolation technique may partially account for the reduction in the prevalence of *Mycobacterium africanum* observed in several West African countries.

PD-610-27 Nationwide molecular typing of *Mycobacterium tuberculosis* complex among retreatment cases in Benin, West Africa

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Background: Molecular epidemiology studies of tuberculosis (TB) are helpful to better understand the dynamics of TB transmission for its control in a given area. However, data on molecular typing of *Mycobacterium tuberculosis* complex are scarce in Africa; data available are either limited to new TB cases, or geographically to an hospital or a region. Nationwide molecular studies on TB retreatment cases are rare.

Methods: A routine sample transportation system from all TB diagnosis centers to the National Reference Laboratory (NRL) has been set up for years in the country: all smear positive retreatment cases are sent to the NRL for culture and drug susceptibility testing (DST). All isolates are stored and the present study was retrospectively performed on isolates obtained in 2014. DNA was extracted by boiling followed by spoligotyping. Data obtained were entered in TB lineage database for lineage determination, and in SPOTCLUST and SITVIT databases for family determination.

Results: In 2014, 193 retreatment cases were identified in the country. Excluding negative culture and non tuberculous mycobacteria, 100 isolates belonging to patients from all the 6 regions of the country were available for spoligotyping. In total, 71% were relapse, 24% were failure and 5% return after default. All except one patient were tested for HIV and 15% were HIV positive. Resistance to rifampin was 14 % and MDR 12%. Among rifampin resistance strains, two were resistant to fluoroquinolones, one to aminoglycosids and none was XDR. In total, 40 different spoligotypes were observed; among them, 21 were previously described while 19 were new. Most frequent spoligotypes were ST 61 (33%) followed by ST 53 (13%) and ST1 (Beijing) (8%). There was no statistical significant association between spoligotypes and HIV, nor with MDR. However, ST1 (Beijing family) was strongly associated with resistance to streptomycin ($P = 0.0001$). Lineages 5 and 6 (*M. africanum* family) was 13% and one strain was *M. bovis*. **Conclusion:** As in previous studies in new cases, ST 61 was the most frequent spoligotypes among retreatment in Benin and Beijing family (ST1) was associated with resistance to Streptomycin. However, unlike previous studies, the second most frequent spoligotype was ST53.

02. Integration of services: attitudes and lessons learned

PD-611-27 Knowledge of tuberculosis and treatment adherence among people living with HIV/AIDS and tuberculosis in Ibadan, Nigeria

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Background: Tuberculosis (TB) not only makes it more difficult for people trying to come to terms with HIV but it also interferes with attempts to fight the AIDS epidemic as a whole. Awareness and knowledge of People Living with HIV/AIDS (PLWHA) and TB have not been adequately investigated. This study therefore assessed knowledge of TB and treatment adherence among PLWHA and TB receiving care at the University College Hospital, Ibadan, Nigeria.

Methods: The cross-sectional study involved the use of a four-stage sampling technique to select 127 respondents who are living with HIV/AIDS and TB. Respondents were interviewed using a pretested semi-structured questionnaire which focused on knowledge of TB and treatment adherence. A 20 point knowledge scale was used to measure respondents' knowledge of TB. A correct knowledge attracted two points while a wrong knowledge was zero. A score of ≤ 14 and ≥ 15 points were considered poor and good knowledge respectively. Data were analyzed using descriptive statistics and χ^2 test.

Results: Mean age of respondents was 32.0 ± 9.4 years, 59.1% were females and 92.9% were tested positive to HIV before developing TB. Respondents mean knowledge score of TB was 12.9 ± 4.4 . Many (56.9%) of the respondents did not know that PLWHA are at greater risk for TB and only 8.9% knew that children can be vaccinated against TB. Almost all (97.2%) of the respondents knew that TB is spread through coughing and sneezing but 32.4% did not know that children living with HIV are at higher risk for serious TB disease. The mean knowledge score of respondents with no formal, primary, secondary and tertiary education were 7.8 ± 4.8 , 8.9 ± 2.6 , 10.3 ± 4.7 and 15.6 ± 3.8 points respectively ($P < 0.05$). Many (47.8%) of the respondents reported non-compliance with TB management and reasons included stigmatization (80.9%), negative attitude of the health care provider (29.8%) and lack of social support (23.1%).

Conclusion: Respondents had a poor knowledge of tuberculosis and non-compliance to management of the disease was also high. Tuberculosis education has a potential for ameliorating the problem.

PD-612-27 Assessment of facility readiness to provide integrated services for HIV and TB in Namibia

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Background and challenges to implementation: In 2014, 44% of TB patients in Namibia were HIV-infected. HIV and TB services have hitherto been provided in separate clinics with inefficient referral systems between the two services. Integrated service provision is being promoted internationally as a way to improve co-management of TB and HIV as well as to improve treatment adherence. Namibia is gradually adopting this approach, but facility readiness to provide integrated services is crucial to the success of this approach.

Intervention or response: An assessment was conducted at 37 health care facilities using a standardized questionnaire. Variables assessed include facility operations, human resource capacity and training needs, provision of quality care, as well as monitoring and evaluation. Additionally, interviews with health care workers (HCWs) on current practices were done and health records of cases registered in October 2015 reviewed.

Results and lessons learnt: Integration of services is not happening at most of the facilities with services being introduced as either TB or HIV; making integration a secondary activity. Only 3 TB facilities have fully integrated HIV care services; 10 partly with integration of any nature could not be reported in the other 24 sites. TB services are generally available at all facilities, but some ARV providing clinics are not initiating anti-TB medicines in favour of TB infection control. HIV services are generally available, with the notable failure to provide HIV counselling and testing (HCT) at DOT points.

Conclusions and key recommendations: Efforts should also be made to train cadres who are strictly providing TB or HIV services to be able to provide integrated services and possibly revise their scope of work to reflect integration. Community based TB DOT points should be equipped to provide to HIV counselling and where feasible testing as well. Implementation of TB infection control measures should be strengthened at all sites. Utilization of services at lower level facilities such as DOT points should be advocated for thus relieving congestion at other facilities.

PD-613-27 Extent of HIV co-infection and provision of services among TB patients in Myanmar

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Background and challenges to implementation: In 2014 the estimated tuberculosis (TB) prevalence in Myanmar was 457 per 100 000 population and the estimated human immunodeficiency virus (HIV) prevalence among ≥ 15 year olds was 0.54% of the general population. Services to TB patients are provided at TB clinics run by either the vertical TB teams and township public health departments (79%), or Public-Public-Mix (PPM) hospitals (4%), or local and international non-governmental organizations (NGOs) (17%). HIV counseling and testing (HCT), cotrimoxazole preventive therapy (CPT) and referral for antiretroviral therapy (ART) services are provided by the National Tuberculosis Programme (NTP) but they still need to be evaluated. The objective of this study is to assess the countrywide situation of HIV co-infection and provision of services among TB patients in Myanmar.

Intervention or response: Since 2014, NTP has registered TB-HIV co-infected patients who attended TB clinics in the whole country including non TB-HIV collaborative townships. Data from January 2014 to September 2015 was used to determine the level of TB-HIV service provisions among TB-HIV patients.

Results and lessons learnt: A total of 249 957 TB patients of all forms were treated in the whole country. Of these, 54% received the HCT service, of whom 15% were HIV positive, among whom 75% were given CPT and 46% received ART. The corresponding percentages reported by NTP including township public health departments were 55%, 9%, 67% and 31%, respectively. For PPM hospitals the reported percentages were 76%, 75%, 97% and 60%, respectively and for NGOs 45%, 22%, 66% and 63%, respectively.

Conclusions and key recommendations: HIV positivity among TB patients of all forms in Myanmar is quite high. Nonetheless, the coverage of HCT, CPT and ART provision is still deficient. The investigation for the root causes of these service inadequacies are needed in order to improve the service provision.

PD-614-27 HIV testing among TB patients rises from 2% to 70% in 7 years in Jharkhand, India

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Background and challenges to implementation: India ranks second in the world and accounts for about 10% of the global burden of HIV associated TB. The Global TB

Report 2015 estimates HIV-TB incidence of 0.12 million and mortality of 0.038 million per annum. Four-pronged strategies, Prevention, Early detection, Prompt Treatment and Management of Complications, have been adopted to reduce the mortality. Jharkhand, India, a tribal (26%) state with population of 35 million, implements TB-HIV strategy even in its remotest part. HIV testing among TB patients was a major challenge across the state. This paper gives the outcome of TB-HIV in a tribal setting.

Intervention or response: Jharkhand introduced intensified TB-HIV programme in 2011. All District Tuberculosis Officers (DTOs) were designated as the Nodal Officer and 'Sr. DRTB-HIV Supervisor' position is in place in all 24 districts for supervision and monitoring of TB-HIV activities. The designated microscopy centres were linked with ICTCs or further designated as Facility ICTCs in collaboration with Jharkhand AIDS Control Society (JSACS) for HIV testing of TB patients. 11 districts were provided with CB-NAAT machines for TB testing of HIV positive chest symptomatic.

Results and lessons learnt: Out of 24 districts in the state, 7 (30%) districts have 100% colocated DMC and HIV testing facilities which also performs equally well in testing all TB patients. 34 792 TB cases were notified from the public sector. Among these, 24 404 (70%) were tested for HIV in 209 (64% of total DMC) co-located TB-HIV testing facilities. Among the tested nearly 1% were found to be HIV positive. The number of testing in 2008 was 2% of 36 543 TB patients identified, which has gone up to 70% during the last 7 years. More than 85% of all TB-HIV co-infected patients were put on treatment. **Conclusions and key recommendations:** Co-location and multi-tasking of TB-HIV testing are absolutely necessary for increasing the TB-HIV testing. In hard to reach and extremist areas like Jharkhand, multi-tasking of technicians has resulted in increasing the testing significantly. The framework need to reinforce the collaborative care to the diagnosed HIV-TB along with testing to prevent the TB further.

PD-615-27 Assessment of uptake of antiretroviral therapy among HIV-infected TB patients in Nigeria

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Background: Tuberculosis (TB) is the leading cause of morbidity and mortality among people living with HIV (PLHIV). Survival benefit due to early (8 weeks) initiation of antiretroviral therapy (ART) among HIV-positive TB patients has been demonstrated. WHO guidelines and the Nigeria National TB-HIV implementation guidelines recommend early initiation of ART in all HIV-positive TB patients irrespective of CD4 count.

We assessed the uptake and timing of ART initiation among HIV-positive TB patients in selected TB and HIV treatment facilities in Nigeria to identify challenges and provide recommendations to improve ART uptake.

Methods: A retrospective review of TB and HIV clinical records for TB patients enrolled at Directly Observed Treatment (DOT) facilities in two of the 37 States in Nigeria (Federal Capital Territory and Ogun) between 1 October 2012 and 30 September 2013 was conducted. All HIV-positive TB patients identified were traced to HIV care and treatment facilities to ascertain their treatment status and timing of ART initiation relative to TB treatment. In-depth interviews were also conducted with key health care workers to assess provider perceptions about the barriers to provision and uptake of ART.

Results: Among 640 HIV-positive TB patients evaluated, 98 (15.3%), (95%CI 12.5–18.1) started ART before TB treatment while 290 (45.3%), (95%CI 39.6–51.0) were not initiated on ART during the course of TB treatment. One hundred and fifty four (24.1%), (95%CI 20.7–27.4) started ART within 8 weeks of TB treatment while 98 (15.3%), (95%CI 12.5–18.1) started ART after 8 weeks of TB treatment. Major challenges to early ART initiation among HIV-positive TB patients include patient delays in seeking care, limited access to ART services for patients diagnosed in peripheral DOT sites as well as poor service linkages in ART/DOT co-located sites.

Conclusions: A large proportion of HIV-positive TB patients were not initiated early on ART in spite of proven survival benefit and longstanding recommendations. Fully integrated TB and HIV service delivery and interventions to strengthen referral systems from peripheral DOT to ART sites should be implemented to ensure timely provision of ART among HIV-positive TB patients in Nigeria.

PD-616-27 Assessment of uptake of antiretroviral therapy among HIV-infected TB patients in Namibia

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Background: Tuberculosis (TB) is the leading cause of morbidity and mortality among people living with HIV (PLHIV). The World Health Organization (WHO) recommends initiation of antiretroviral therapy (ART) within 8 weeks of starting TB treatment for all co-infected patients. Namibian guidelines have included these recommendations since 2010, but implementation is unknown.

Methods: This study aimed to assess the timing of ART initiation for TB-HIV co-infected patients in Namibia. A

retrospective cohort analysis was done using paper-based and electronic data sources. All patients registered at fifty TB facilities in 8 health districts between October 1, 2011 and September 30, 2012 were included. TB treatment information was abstracted from the TB registers. Patients with an HIV status of positive or unknown were matched when possible to their HIV records for collection of more detailed HIV and ART-related information.

Results: From 5,003 TB patients, 2276 (45.4%) were documented as HIV positive; 391 (7.8%) had unknown HIV status. Among TB-HIV co-infected patients, 966 (42.4%) were enrolled for HIV care and treatment. Of these 265 (27.4%) initiated ART prior to TB diagnosis and 458 (47.4%) patients had missing documentation of ART status at the time of TB treatment initiation; these patients were excluded from further analysis. ART was initiated in the majority (235, 96.7%) of the remaining 243 patients not on ART at the time of TB treatment initiation. Timing of ART initiation was known for 186 (79.1%) of these patients, among whom 92 (49.5%) started ART within 8 weeks of starting TB treatment.

Conclusions: Namibia has a high TB-HIV co-infection rate. Fewer than half of the HIV positive TB patients could be matched to HIV care indicating inadequate linkages between programs. While ART initiation among co-infected patients is high, many patients did not start ART within the recommended 8 weeks. Additionally, limitations of the current data systems pose challenges to following care for TB-HIV patients. It is recommended to strengthen clinical and data linkages between TB and HIV services in order to ensure that co-infected patients receive timely care and treatment.

PD-617-27 TB-HIV service integration among co-infected patients in Kapkatet district hospital

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Background: TB-HIV co-infection among TB patients tested for HIV stands at 41% in Kenya. At Kapkatet district hospital, there was a 26% co-infection rate as of 2012. TB-HIV services at Kapkatet hospital started in 2005 and was supported by PEPFAR Program. TB clinic was approximately 100 meters away from HIV clinic. Despite existence of referral mechanism patient got lost in the process due to distance, time and stigma. This contributed to low uptake of ARTs at 9.5% (2012) and increase in number of defaulters while treatment success was at 62% which contributed to resistance of ARVs. In order to address the challenges faced; the hospital management had to set up integrated TB-HIV services under one roof.

Intervention: A TB-HIV collaboration committee was formed in 2012 comprising TB-HIV stakeholders and hospital management. In 2013, the committee identified challenges and solutions by a review of clinic data. One of the major challenge was the separation of TB and HIV clinics. TB-HIV drugs were integrated as compre-

hensive services including OIs management in the same room.

Results and lesson learnt: ART uptake increased from 9.5% in 2012 to 96% in 2014, adherence to anti-TBs went from 70% in 2012 to 94% in 2015. Out of the 51 co-infected patients, treatment success was at 98% and viral load suppression was at 90. These results were attributed to integration of service and regular follow up of the patients.

Conclusion and key recommendations: Integration of TB-HIV at public hospital improve treatment success of TB co-infected patients. Setting up a functional mechanism of collaboration facilitate out the integrated services. The integration of this do not necessarily require additional health care workforce but ensure continuation of care to patient by building confidence on existing healthcare providers this reduce stigma thus improving adherence for the patient.

PD-618-27 Administrative interventions increase antiretroviral initiation in patients with HIV and drug-resistant tuberculosis in the co-epidemic region of Irkutsk, Siberia

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Background: At the tuberculosis (TB) referral hospital in Irkutsk, Russian Federation, we conducted an impact assessment of interventions designed to integrate the provision of human immunodeficiency virus (HIV) and TB services on antiretroviral (ART) utilization.

Methods: A pre and post-intervention study was conducted for HIV-infected patients admitted for TB treatment from February 2014 to December 2015. Interventions included: reducing the time between the first and subsequent follow-up by specialists, creation of a new managerial position within the Irkutsk TB Dispensary to coordinate care with the HIV services center, onsite CD4 count and viral load testing to reduce the time to action on HIV laboratory results, and administrative prioritization of referrals for ART from the TB hospitals to hasten committee approval and dispensation of ART. Quantitative HIV and TB outcomes and qualitative interview of providers were used to assess effectiveness.

Results: A total of 193 TB-HIV co-infected patients were identified during February 2014–December 2015 of whom 157 (81%) were ART naïve and 73 (46.4%) had multidrug-resistant TB. During the pre-intervention 2/2014–8/2014, 78 ART naïve patients were enrolled with a median CD4 count of 147 (45–256) per mm³. From 4/2015–12/2015, 79 ART naïve patients were enrolled with a median CD4 count of 55 (25–163) per mm³. ART utilization rates in ART naïve patients increased signif-

icantly from only 10 (13%) during 2/2014–8/2014 to 46 (58%) in 4/2015–12/2015 ($P < 0.001$). Excluding those with refusal or early death, 46 out of 59 (78%) post-intervention patients were started on ART. Furthermore, the time to ART initiation decreased from a median of 543 (531–555) days in the pre-intervention patients to 80 (53–110) days. Similarly, 21 (27%) of pre-intervention patients were not started on ART because of TB treatment interruption or transfer to another facility, compared to 7 (9%) of post-intervention patients ($P = 0.003$). Qualitative interview with TB providers identified administrative prioritization as the most important factor in increasing ART utilization.

Conclusions: Administrative interventions to integrate HIV and drug-resistant TB services significantly increased ART initiation in a co-epidemic region of Siberia. Additional studies are regionally necessary to close further the gap in ART initiation and support TB treatment completion.

PD-619-27 Improving the quality of integrated TB-HIV health care services through dual SIMS tool administration and capacity building: experiences from Kebbi State, Nigeria

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Background and challenges to implementation: The provision of quality healthcare services to PLHIVs is necessary for the reduction of HIV-related morbidity & mortality but this has remained a challenge in resource-constrained settings including Nigeria. Management Sciences for Health (MSH) implements the USAID-funded ProACT Project which supports comprehensive HIV care and treatment services in Northern Nigeria. Specific challenges noted at baseline assessments of Sir Yahaya Memorial Hospital (SYM), a government-owned secondary health facility in Kebbi State, were poor documentation of ART initiation in confirmed adult TB patients, lack of an infection control plan and no designated facility cough officers. MSH conducts facility-level administration of the SIMS (Site Improvement through Monitoring Systems) Tool which assesses adherence to PEPFAR standards of service delivery by revealing programmatic gaps and conducts capacity-building of healthcare workers to provide quality services through targeted mentoring.

This paper examined the effect of the dual approach of SIMS Tool administration at periodic facility support visits and targeted mentoring, on improving the quality of integrated TB-HIV service delivery at SYM.

Intervention or response: A baseline assessment on 09/06/2015 revealed 30% of HIV-positive adult TB patients had documentation of ART initiation in the TB Register; lack of designated facility cough officers and lack of a facility infection control plan. The interventions implemented were mentoring of the DOTS focal person on appropriate documentation in the TB Register, the

nomination and training of a cough officer and the development and implementation of an infection control policy. Subsequent assessments were conducted on 15/07/2015 and 02/10/2015 to assess the same service delivery elements.

Results and lessons learnt: Documentation of ART initiation in HIV-positive adult TB patients increased to 70%, a cough officer was available and seen fast tracking, triaging and separating coughers, and an infection control plan sighted. Documentation of ART initiation in HIV-positive adult TB patients increased to 80% by the 3rd visit.

Conclusions and key recommendations: The dual approach of the SIMS Tool administration and targeted capacity-building of key facility healthcare workers led to progressive improvements in quality integrated TB-HIV healthcare service delivery. The success of this intervention presents opportunities for its future implementation across other healthcare programmes

PD-620-27 Improved TB-HIV collaborative activities via health system strengthening in two regions of Ethiopia

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Background: We present the progress in key TB-HIV collaborative activities in two regions of Ethiopia, which were supported by the USAID funded Help Ethiopia Address the Low TB Performance (HEAL TB) project since July 2011.

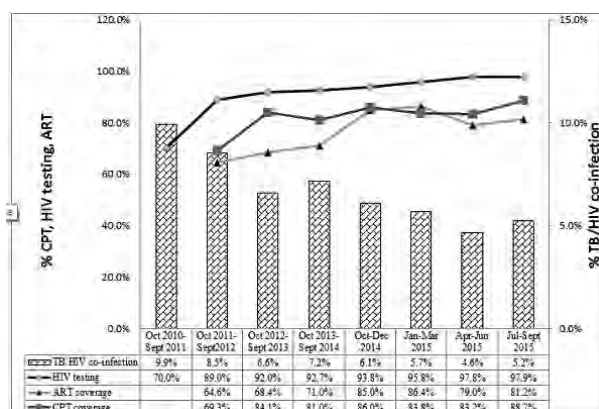
Interventions: Health workers were trained on the comprehensive TB-HIV management. Regular mentoring and supportive supervision were also made through the district health system. The project provided job aids and supplies, and ensured adequate supply of test kits, laboratory supplies and medicines through the government system. Poorly performing health facilities were placed on a performance improvement plan and closely monitored every three months.

Results and lessons learnt: The proportion of TB patients tested for HIV increased from 70% in October 2011 to 98% in September 2015. The percentage of newly diagnosed TB-HIV co-infected patients put on ART has reached 81.2%, from 64.6% in October 2011. Cotrimoxazole preventive therapy (CPT) uptake rate improved from 69.3% to 89%. During the four years period, the TB-HIV co-infection rate has declined by 47.4% (from 9.9% to 5.2%) [Figure]. An ordered trend test over four years shows that there is a significant declining trend of TB-HIV co-infection ($Z\text{-Score} = -2.52$, $P = 0.012$) along with a significant increment in the trend of HIV testing ($Z\text{-Score} = 2.65$, $P = 0.008$) and ART coverage ($Z\text{-Score} = 1.92$, $P = 0.054$).

Conclusion: Capacity building of health care workers through training and regular mentoring is effective intervention in improving TB-HIV collaborative activi-

ties. The reduction in TB-HIV co-infection rate can be attributed to the increased ART coverage in the HIV program that likely prevented the occurrence of opportunistic infections including TB.

Figure Trend of TB-HIV performance



PD-621-27 Integration of isoniazid preventive therapy into routine elimination of Mother-to-Child transmission (eMTCT) HIV services in a Ugandan urban health facility

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Background: Isoniazid preventive therapy (IPT) policy was rolled out in 2014 targeting eligible people living with human immunodeficiency virus (PLHIV) and prioritizing PLHIV newly enrolled in HIV care. Although the Ugandan Ministry of Health (MoH) recommends IPT among pregnant women living with HIV, there are no guidelines on integrating tuberculosis (TB) services into maternal, neonatal and child health (MNCH) services. In August 2015, the CDC/PEPFAR-funded Infectious Disease Institute (IDI)-Kampala Capital City Authority (KCCA) project supported Kitebi health center three (HC III) in Kampala to integrate IPT into routine elimination of mother-to-child transmission (eMTCT) services. This paper presents outcomes of pregnant women living with HIV initiated on IPT at this facility.

Intervention: As part of phased-implementation of IPT, IDI-KCCA trained Kitebi HCIII midwives based in eMTCT and early infant diagnosis (EID) clinics on the national IPT implementation guidelines. Job aides and IPT register were provided. All midwives agreed to participate in identification of eligible clients, counseling,

initiation, documentation and follow up of clients on IPT. IPT initiation was based on available facility stock of isoniazid. Logistics management and facility-community linkage were integrated into existing systems at the facility. Targeted mentorship visits were conducted to support IPT implementation in eMTCT/EID clinics.

Results: Between August and September 2015, 23 (30%) out of 76 newly enrolled into HIV care eligible pregnant women living with HIV were initiated on IPT at Kitebi HCIII. They ranged between 18 and 37 years of age with 61% below 25 years. About 96% (22) of them had a telephone contact and 70% (16) lived within the 5 km radius to the facility. 74% (17) of these successfully completed their 6-month doses of isoniazid and 26% (6) were lost to follow up (LTFU). Reconciliation of data in the client files with the IPT register improved completion rates in the register from 35% to 74%. Through phone call follow up, it was ascertained that the six clients that were LTFU self-referred to rural HIV clinics for postnatal care.

Conclusions and key recommendations: IPT was successfully integrated into eMTCT/EID services. Lessons learnt can inform integration of TB services into MNCH services.

PD-622-27 Pattern of TB-HIV co-infection among people living with HIV/AIDS: economic importance of IPT in supported health facilities in Northern Nigeria

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Background: Isoniazide Preventive Therapy remains an essential care package offered to People Living with HIV/AIDS who screen negative to TB symptoms as a prophylaxis to TB infection. Evidence has shown that the intervention is capable of protecting against TB for a maximum of 60 months if a 6 months course of therapy is completed. Nonetheless, according to the World Health Organization, TB remains an important cause of death and carries an associated high cost of treatment at \$2000 per patient among PLHIV. USAID funded MSH-Pro-ACT project took to scale IPT intervention through her IPT TB Burden Reduction program in July 2013. The objective of this paper is to assess the effect of this intervention on the rates of TB among PLHIV and economic importance of IPT.

Method: The project scaled up IPT intervention by developing a package encompassing of; structured continuous medical education of health care workers; pre-packing of IPT into 6 months individualized patients kits; synchronizing IPT prescription with ART refill and clinic attendance; training and retraining of health care workers on IPT use; and conduct of bi-annual process evaluation. Data review was conducted in 2015 December to determine the prevalence of TB co-infection pattern among PLHIV.

Results: Before the introduction of IPT, 9.2% (30/326) of PLHIV who are in care and on ART were diagnosed with TB. At the same period 3.7% (21/573) of PLHIV were diagnosed with TB from the DOTS services center. However, with the introduction of IPT, 1.4% (13/941) of PLHIV who commenced IPT and are on ART were diagnosed with TB while at the DOTS services center 6% (31/513) PLHIV were diagnosed with TB

Conclusion: Taking IPT to scale and offering HAART at the point of HIV diagnosis could be the magic bullet for the desired turning point in TB epidemic among PLHIV in high burden countries. The review also showed that 12 TB cases were averted which translate to over \$34 000 thus providing evidence of economic importance of IPT. Furthermore, reactivation is implicated as a major cause of TB among PLHIV. Strengthening DOTs services HIV screening will enhance co-epidemic management.

03. Childhood asthma and TB: a potpourri

PD-623-27 Care givers' asthma knowledge and quality of life in asthmatic children requiring re-attendance for emergency care with acute asthma in Esmeraldas, Ecuador

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Background: Asthma exacerbations are common and are associated with substantial morbidity and a risk of death, especially in low-resource settings. Asthma education interventions reduce emergency care reattendance for acute asthma, though there is less certainty over the influence of caregiver asthma knowledge. Poorer quality of life (QoL) has been associated with a greater risk of asthma exacerbations. We aimed to explore the effect of asthma-related QoL and asthma knowledge on future risk in asthmatic children in a low-resource setting.

Methods: We undertook a prospective cohort study at the public hospital and health centres in Esmeraldas City. Children aged 5–15 years presenting to the ER with acute asthma were followed-up for 6 months to document number and severity of subsequent asthma attacks. Here we present the results of the carers' Newcastle Asthma Knowledge Questionnaire (NAKQ) scores and the children's Pediatric Asthma Quality of Life Questionnaire (PAQLQ) scores, divided into three domains (symptoms, activity and emotional).

Results: 283 children were recruited over 17 months, of whom 263 caregivers completed the NAKQ, with a median score of 18 (of 31) (IQR 16–20). The median score for the PAQLQ completed by 222 children was 3.5 (IQR 3.0–4.0), of a 1–7 scale, the lower score representing a poorer QoL. The median scores for each PAQLQ domain were: symptoms 3.5 (IQR 2.8–4.1); activity 3.4 (IQR 2.6–4.0); emotional 3.7 (IQR 3.1–4.5). A high

NAKQ (OR: 0.91, 95%CI 0.85–0.98) and PAQLQ emotional domain (OR: 0.72, 95%CI 0.55–0.94) score were associated with a lower risk of subsequent asthma attacks requiring emergency care. We found no significant association between PAQLQ total score, symptoms or activity domain, and future risk.

Conclusions: Asthma specific knowledge was low among carers of asthmatic children visiting an ER for an acute asthma attack, and the lower the score, the higher the risk of subsequent ER re-attendance. Only a poor score on the emotional domain of the PAQLQ showed an increased risk of future asthma attacks requiring emergency care. There appears scope to improve the outcomes of asthmatic children in this setting through educational interventions.

PD-624-27 Asthma control among children aged 5–17 years attending Mulago Chest Clinics

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Background: Uncontrolled childhood asthma affects the child's growth and development, and overall quality of life, and is associated with avoidable high healthcare costs. The aim of this study was to document the level of asthma control in children at Mulago National Referral Hospital and describe factors associated with asthma control.

Methods: A cross-sectional descriptive study of 91 children aged 5–15 years with documented persistent asthma was done between June 2014 and January 2015 at the paediatric and adult chest clinics of Mulago hospital. Asthma control was determined using an interviewer-administered questionnaire that was compared to the GINA guidelines and the Asthma Control Test (ACT). The caretakers' perception of their child's asthma control was also assessed. Logistic regression analysis was used to determine the factors associated with asthma control.

Results: Of the 91 children studied, 51 (56.0%) were males, and the mean age was 10.2 years. Twenty (22.0%) of the participants had controlled asthma based on the GINA guidelines. Using the ACT, only 16 (17.6%) children were found to have controlled asthma. Sixty four (70.3%) of the 91 parents/caretakers considered their children's asthma well controlled, yet only 56.0% of them were uncontrolled on assessment using the GINA guidelines. Age of the child (COR 1.2, 95%CI 1.05–1.38, $P=0.006$), duration spent on medication for asthma (COR 0.7, 95%CI 0.05–9.21, $P=0.017$), mother's education level (COR 0.7, 95%CI 0.23–2.21, $P=0.009$) and presence of an allergic skin rash (COR 2.7, 95%CI:0.99–7.16, $P=0.043$) were the factors that were significantly associated with good asthma control. However, only a higher level of education of the mother was independently associated with good asthma control.

Conclusions: A large proportion 71 (78.0%) of children attending Mulago Chest Clinics have uncontrolled asthma. The factors associated with uncontrolled asthma are; young age of a child less than 8yrs, mother's education level below tertiary, duration of less than 2 years on asthma medication and presence of an allergic skin rash. In-depth studies on asthma control in children and associated factors should be carried out in Mulago Hospital.

PD-625-27 Impact of training in childhood TB in Bangladesh: a rapid assessment report

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Background and challenges to implementation: The actual disease burden of childhood TB in Bangladesh is unknown. Only a small proportion of the estimated childhood TB cases are diagnosed. According to NTP data, only 3% of the notified cases is child TB while the global estimated incidence is 10–20%. Lack of skilled providers across the health care system is one of the reasons for low level of detection of childhood TB cases in Bangladesh.

Intervention or response: To address this challenge, the TB CARE II project took the initiative to develop a partnership with the Bangladesh Pediatric Association (BPA) for training of pediatricians, doctors, general physicians and health care workers. Through this partnership, the project developed 38 medical professionals as trainers and supported training of 1,168 doctors and also facilitated these doctors to orient a total of 8345 health workers on contact tracing, screening and referral of presumptive child TB cases. The project conducted a rapid assessment to determine the outcome of the childhood TB training. The data was collected from 22 randomly selected health facilities which were covered through this training.

Results and lessons learnt: According to assessment findings, 67% of the respondents correctly mentioned the proper diagnostic procedures as taught in the training. 97% of the respondents practice correct procedures for diagnosis of TB in children. The results indicate that the training was effective to improve service providers' skills and practice for correct diagnosis of child TB. The childhood TB case detection increased by 30% compared to the baseline period (January–June 2013). Case detection has increased by 25% for the 0–4 years age group and by 25% for the 5–14 years age group.

Conclusions and key recommendations: A structured child TB training is critical for improving service provider's knowledge and skills for improved management of child TB and increasing notification which is very low in Bangladesh. The training should be conducted with greater emphasis on building a team approach amongst the public, private and NGO sector providers for improved local level planning, program-

matic collaboration, monitoring and supervision and better outcomes.

PD-626-27 Evaluating the capacity of clinicians to assess children for TB, and need for isoniazid preventive therapy in Uganda: opportunity for quality improvement

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Background: Owing to suboptimal performance of tuberculosis (TB) diagnostic tests in children, TB diagnosis largely relies on clinical assessment yet few clinically diagnosed cases are notified in Uganda. Assessment of TB is done by clinical officers and nurses whose knowledge of child TB diagnosis has not been evaluated. Eligible children are rarely initiated on Isoniazid preventive therapy (IPT) despite being a national guideline. We aimed at assessing capacity of clinicians, nurses to evaluate children for tuberculosis, need for IPT in Kampala.

Methods: In this cross sectional study, we reviewed patient record forms (PRF) of 1999 children aged below 15 years, attending 4 health facilities in urban slums of Kampala, September 2015 to March 2016. Socio-demographic, clinical, and laboratory data extracted from PRFs. TB diagnosis was assessed based on the 'Desk Guide for diagnosis and management of paediatric TB' clinical algorithms. Cardinal symptoms: chronic cough, fever for over two weeks, weight loss, TB contact history, less playfulness. Sputum analysis based on microscopy and/or GeneXpert. Eligibility for IPT based on Ministry of Health guidelines. Analysis using stata 13, adjusted for clustering.

Results: Mean age 4.3 ± 4.1 years with 1004 (51.7%) being females. In 286 (14.7%) children, clinicians did not assess for any of the cardinal symptoms suggestive of TB while only 383 (19.1%) had all the symptoms assessed (Table). Overall, 579 (29.0%) children were presumed to have TB. Of these, only 2 (0.1%) had sputum examination requested and 6 (0.3%) had HIV test done none of which was positive. Only 5 (0.3%) children were referred for further evaluation. No child was diagnosed with TB despite 27 (1.4%) children meeting the criteria for clinical TB. None of the 3 (0.2%) patients eligible for IPT was identified thus not initiated on isoniazid. In 232 (11.6%) of patients, no diagnosis was given.

Conclusions: Fundamental gaps exist in pediatric TB evaluation during primary health care (PHC) delivery in Uganda, including symptom-screening, diagnosis, and preventive treatment. Multiple missed opportunities for early diagnosis and prevention of TB in children. Clinical TB guidelines need to be optimized at PHC facilities.

Table Missed opportunity for symptom screening among 1999 children

	Missed symptom n (%)
Symptoms not assessed for by clinicians	
Cough for >10 days	373 (34.1)
Drenching night sweat	455 (22.8)
Fever lasting >10 days	354 (33.2)
Contact with confirmed adult TB patient	444 (22.2)

Evaluation for TB among 1999 children <15 years

Variables	n (%)
Patient presumed to have TB (has at least one symptom)	579 (29.0)
HIV test because patient is presumptive	6 (0.3)
Sputum test ordered	2 (0.1)
Patient meets criteria for clinical TB diagnosis	27 (1.4)

PD-627-27 Managing childhood TB in a high-burden district in South Africa: getting the basics right

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Background: The paucibacillary nature of childhood tuberculosis and challenges in obtaining samples result in the majority of children being treated and monitored for TB based on clinical criteria. The South African National TB Program (SANTP) has established guidelines for diagnosis and management of childhood TB. We evaluated the implementation of these guidelines at primary care clinics (PCC) in the Eastern Cape Province, South Africa

Methods: Retrospective TB folder review of children ≤14 years of age, recorded in the Electronic TB register (ETR) during 2014 in six high-burden PCC.

Results: A total 280 children (13% of total caseload) were recorded in ETR; 208 (74%) ≤5 years of age, 46 (16.5%) HIV-infected and 268 (96%) with pulmonary TB. Folders for 252 (90%) were reviewed. Diagnostic symptoms and signs were documented for only 18 (7%); information on TB exposure in only 44 (18%) children. HIV status was documented in 211 (84%); only 23/36 (64%) infected children were documented to have started antiretroviral therapy. Only 27/66 (41%) of children aged 6-14 years had samples taken for bacteriological testing. Of 209 children (83%) who had weight and treatment dose recorded at treatment initiation, only 122 (58%) received the correct weight-banded dosage. Weight at the start of continuation phase was documented in 133 (53%). Favourable treatment outcomes were documented in 192 (75%) of children

Conclusions: Results from this audit highlight important policy-practice gaps. Lack of systematic documentation of clinical findings and decision-making, i.e. weight and laboratory investigations; impacts negatively on optimal treatment, and monitoring of treatment response in

children. Despite 75% of children completing treatment, incorrect dosing of TB treatment could have a negative impact on long term treatment success in terms of relapse and resistance. New tools including better diagnostics and more child-friendly regimens will fail to have significant impact on childhood TB globally if basic TB management principles in children are neglected.

Overview of observed childhood TB management practices by key management activities according to 2013 national TB guidelines at 6 high-burden TB clinics in Nelson Mandela Metro District Eastern Cape, South Africa during 2014 (n=252)				
NTP key activities according to guidelines	Guidelines followed appropriately		Guidelines not followed appropriately	
	n	%	n	%
Diagnostic Criteria				
Clinical signs and symptoms documented at diagnosis	18	7%	234	93%
Information on TB exposure documented ¹	44	18%	208	83%
HIV status documented	211	84%	41	16%
HIV infected	36/211	17%	-	-
Documented ARV treatment	23/36	64%	13/36	36%
Special investigations				
TST done ²	82	33%	170	67%
CXR done for children with Pulmonary TB	197/243	81%	46/243	19%
CXR reported ³	185/197	94%	12/197	6%
CXR suggestive of TB	183/197	94%	14/197	7%
Pathogenomic signs reported	24/197	12%	173/197	88%
Respiratory specimen sent for bacteriological testing ⁴	35/243	14%	208/243	86%
0-5 yrs	8/183	4%	175/183	96%
6-14 yrs	27/66	41%	39/66	59%
Treatment initiation				
Weight documented at start of Intensive Phase	234	92%	18	7%
Starting Treatment ⁵ dose and weight documented	209	83%	43	17%
Dose according to weight banded dosing ⁶ chart	122/209	58%	87/209	41%
Unknown starting dose and/or weight	-	-	43/252	17%
Follow-up				
Weight and symptoms documented at 1 st follow-up visit	88	35%	164	65%
Weight and symptoms documented at 2 nd follow-up visit	77	31%	175	69%
Weight documented at start of Continuation Phase	133	53%	119	47%
Treatment outcome				
Treatment completed	192	76%	-	-
Defaulted	23	9%	-	-
Moved out	8	3%	-	-
Outcome not evaluated	-	-	29	12%
Deaths	-	-	-	-

¹ Any clinical symptom or sign documented on TB file that related to diagnosis
² Any index case name or 'no contact with TB case' documented
³ TST has been out of stock in South Africa for a number of months during 2014
⁴ Any doctor interpretation documented in clinical notes on TB file was classified as reported
⁵ Any respiratory specimen - sputum, Gastric Aspirate etc. sent for any bacteriological test - smear, culture, Gene Xpert
⁶ According to the 2013 NTP weight banded dosing charts
 NTP - National TB Program; TB - Tuberculosis; HIV - Human Immunodeficiency Virus; ARV - Anti Retroviral Treatment; TST - Tuberculin Skin Test; CXR - Chest Radiograph

PD-628-27 Paediatric patient support through TB character 'Buddy Beat TB' in South Africa

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Background and challenges to implementation: Innovation is required to address the psychosocial needs of children undergoing treatment for multidrug-resistant tuberculosis (MDR-TB), a particularly difficult journey for children involving prolonged hospitalisation and painful adverse events. Between December 2014 and November 2015, USAID TB Care II South Africa in partnership with Western Cape Department of Health

developed a TB character known as 'Buddy Beat TB' to serve as a companion to paediatric patients on their treatment journey, and to improve knowledge about MDR-TB and to improve treatment outcomes.

Intervention or response: The initiative supported paediatric MDR-TB patients through a model that integrates elements of Play Education Therapy to create a companion for the children, Buddy, who shows solidarity, support and brings some cheer to children on their treatment journey. The character was developed with input from children in MDR-TB hospitals in the Western Cape and Gauteng Provinces, through an Action Media framework, with designing followed by testing in several workshops to enable children to come up with ideas on what their ideal companion would look like. This resulted in Buddy.

Results and lessons learnt: Buddy was successfully introduced to the children during a side-event hosted by the South African Minister of Health and attended by 25 parliamentarians from the Global TB Caucus, at the 46th Union Global Conference in November 2015. The children were enthralled to see their ideas come to life in the form of Buddy, whom they enthusiastically embraced. Positive feedback was also received from care providers and the provincial and district departments of health.

Conclusions and key recommendations: This innovative approach integrated elements of Play Education Therapy to create a companion for the children, Buddy Beat TB, who shows solidarity, support and brings some cheer to the children on their treatment journey.

Figure Buddy Beat TB



PD-629-27 The use of fixed-dose combinations of drugs for treatment of pulmonary tuberculosis in children

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Background: Tuberculosis is still one of the most difficult infectious diseases to treat, especially in children. One reason is the need for long-term use of 3 or 4 drugs, that often causes adverse reactions and psychological stress in children.

Objective: To compare the efficacy and incidence of adverse reactions while use of standard drugs and fixed-dose combinations for treatment of pulmonary tuberculosis in children.

Methods: 46 children from 3 to 14 years old with pulmonary tuberculosis were treated during 2015 at children's phthisiopulmonology department (St. Petersburg Research Institute of Phthisiopulmonology). All children received daily treatment with 4 drugs (rifampicin, isoniazid, pyrazinamide, ethambutol) in the 8-week intensive phase of treatment and were divided in two groups: I group - 25 children who received 4 anti-TB drugs separately; II group - 21 children who received fixed-dose combination of drugs: Isoniazid 150mg+Pyrazinamid 375mg+Rifampicin 150mg (Ftizamax®) and ethambutol. The groups were comparable in terms of clinical, radiological, and laboratory data. Examination was performed before treatment and after 8-week of treatment. Diagnostic complex included: computed tomography, tuberculin skin test, Diaskintest, microbiology methods, real time PCR. Results of examination after 2 months of treatment were compared between the two groups. We evaluated adverse events of treatment. We carried out statistical analysis with the use of the program GraphPad Prizm 6.0. We applied the χ^2 criterion.

Results: Clinical symptoms of intoxication have been decreased after 8 weeks of treatment in the I group in 11 of 25 children (44%) and in the II group in 17 of 21 children (80.9%) ($\chi^2 = 5.74$, $P < 0.05$). Positive dynamics according to X-ray examination was observed in 40% (I group in 61.9% (II group). Adverse reactions to TB drugs (allergic skin reactions, elevated transaminases (ALT, AST), neurological symptoms) were observed in I group in 8 (32%) children. In II group children didn't develop reactions. After intensive phase children were treated by standard combination of drugs (isoniazid, rifampicin/pyrazinamide).

Conclusions: Administration of fixed-dose combination of drugs (Isoniazid 150mg+Pyrazinamid 375mg+Rifampicin 150mg (Ftizamax®) in children with tuberculosis is effective, convenient for intake, and demonstrates favorable pattern of adverse reactions, so it can be recommended for clinical practice.

PD-630-27 Integrating childhood TB care in public-private mix in Pakistan: reaching the unreached

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Background and challenges to implementation: We have seen a stagnant TB case notification in Pakistan both in public and private sector since last few years notifying on an average 300 000 i.e. 60% of the incident cases TB cases annually. The majority (85%) of these cases including almost all childhood TB cases (9% among the notified) are being reported from public sector health facilities. The remaining 15% of the annual TB case notification aged >15 years is from the private sector and other government sector providers such as general practitioners, private hospitals, social security and railway hospitals, etc. This embarks on innovations which can help capture childhood TB cases in the private sector.

Intervention or response: During 2015, a pilot project was implemented by Social and Health Inequalities Network (SHINe), a not for profit private organization in collaboration with provincial TB control programme Khyber Pakhtunkhwa, Pakistan. The project got financial support from EPOS/KfW. The project was implemented in 11 major districts of province in which 75 private providers were selected through a mapping exercise including pediatricians, pulmonologists and general practitioners. They were strengthened by giving training on childhood TB guidelines, free of cost pediatric anti-TB drugs, recording and reporting tools and awareness materials and monitoring support.

Results and lessons learnt: During the total eight months of project period the targeted cases were 900 whereas, a total of 1215 childhood TB cases were reported from the project districts achieving a target of 135%. Most of the cases were reported from big cities such as Peshawar, Swat and Malakand. The training although took more time than anticipated, but helped significantly in structuring the implementation process.

Conclusions and key recommendations: The achievement of targets within a limited time period demonstrates the success of project. The key recommendations includes: a) comprehensive strategy should be developed to address the childhood TB care in private sector, b) a proper estimation methodology is required for the anti-TB drugs for children in the private sector, and c) operational interventions are required to ensure regular reporting of childhood TB case notification and treatment outcomes from the private sector.

PD-631-27 Pediatric TB: reverse contact tracing efforts in a rural setting of Pakistan

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Background and challenges to implementation: Childhood tuberculosis (TB) is a major public health concern in Pakistan. In 2014, 316 577 TB cases were reported in the national TB data of which 27 245 (8.6%) were children. Reverse contact tracing is a strategy used to identify the potential source case in the household of a child diagnosed with TB. Therefore, in addition to routine contact tracing of children living with adults with TB, we also conducted reverse contact tracing of household members of children diagnosed with TB.

Intervention or response: We introduced contact tracing interventions at the pediatric outpatient departments of three large public hospitals in Jamshoro district of Sindh, Pakistan from October 2014 to March 2016. Our protocol was that any household member with one or more suggestive TB symptoms and all 0-4 year olds will undergo a thorough clinical assessment. Although the activity was focused at finding the adult source case in the house, we found that adult family members were less likely to come to the clinic for evaluation. Families were more likely to bring other children in the house for clinical evaluation. Families received travel reimbursement for travel to the health center.

Results and lessons learnt: Over 18 months of program implementation, 1366 children living in the households of 450 children diagnosed with TB were screened. 466 (34%) of those screened were diagnosed with TB and started on treatment. Of those diagnosed 404 (86%) had pulmonary TB, and 254/466 (55%) were younger children (0-4 years). Among adults from the same households, of the 1020 screened, 303 (30%) were identified as presumptive TB cases. Of these only 246 presented for clinical evaluation and 15/246 (6%) were diagnosed with TB and started on treatment.

Conclusions and key recommendations: We found an unusually high TB disease prevalence among other children living in the households of children newly diagnosed with TB. We also found the likely TB source case in some instances, however a concerted effort to identify adult source cases by screening entire households for TB disease is needed for effective TB control.

PD-632-27 Contact tracing in children in northern Stockholm, Sweden, 2000-2014

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Background and challenges to implementation: We describe the evaluation of children at contact tracing before and after the introduction of IGRA tests.

Intervention or response: 1700 children < 18 years old were referred for contact tracing to our pediatric tuberculosis (TB) clinic between years 2000–2014. Interferon gamma release assays (IGRAs) were increasingly used from 2008. Essentially all were managed by one of the authors (RB).

Results and lessons learnt: We evaluated 876 children before (P1) and 824 after 2008 (P2). During P1 we found 39 cases of active TB (including a day care outbreak with 18 cases), 257 of latent tuberculosis infection and 580 were considered uninfected. During P2, there were 12, 125, and 687 children in these categories. Thus 34% were considered infected during P1 and 17% in P2, respectively. Among the 1112 children who were evaluated using TST only, 222/558 (40%) of contacts to smear positive patients and 132/554 (24%) of contacts to smear negative patients had a positive result. Of the 446 children evaluated with IGRA, with or without previous TST, 60/234 (26 %) and 24/212 (11%) had a positive IGRA result.

Conclusions and key recommendations: During P2, the proportion of contacts considered infected decreased by about half compared to P1, probably at least partly due to the higher specificity of IGRAs compared to TSTs. The lower rate of active TB during P2 suggests that other factors, such as earlier diagnosis of index cases, may have contributed to this development.

PD-633-27 A retrospective review to determine neonatal tuberculosis in KwaZulu Natal, 2012–2014

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Background: One third of the estimated 9.6 million people living with tuberculosis, are women. Aligned with the HIV epidemic, the burden of TB is borne by women in the reproductive age group with adverse impact on both maternal and neonatal outcomes widely documented. The extent of neonatal tuberculosis however is largely underestimated as a result of multiple factors including limited diagnostic capabilities and the paucibacillary nature of the disease. The objective of this retrospective review of laboratory records is to establish the rate of drug susceptible and drug resistant TB in neonates in KwaZulu Natal (KZN) between 2012 and 2014.

Methods: All clinical specimens submitted to the National Health Laboratory Service, KZN province for investigation of neonatal TB were evaluated. Auramine O staining followed by liquid culture (MGIT 960) was performed on all samples followed by Ziehl Neelsen (ZN) staining of all culture positive specimens. Genotype MTB-DRplus assay was then done on all AFB positive (with cording cultures) for *Mycobacterium tuberculosis* confirmation and Rifampicin and INH susceptibility testing. Second line DST is subsequently performed on all

resistant isolates. Laboratory data over 3 years was analysed.

Results: *M. tuberculosis* was isolated in 80 samples over 3 years, 33 in 2012, 27 in 2013 and 20 in 2014. Sixty one samples (76.3%) overall were drug sensitive TB strains. A total of 7 monoresistant cases (to either INH or rifampicin) were identified. The prevalence of multidrug-resistant TB (MDR-TB) in these 3 years was 6.0%, 22.2% and 25.0% respectively, resulting in a total of 13 cases (16.3%). One isolate in 2012 showed extreme drug resistance (XDR-TB). The MDR and XDR-TB strains were received from 3 districts within KZN.

Conclusions: A high rate of drug resistance within the neonatal period in KZN was detected in this review. This is reflective of the burden of disease in the adult population, particularly during pregnancy with resultant transmission to the neonate. Three 'hotspots' for MDR and XDR-TB was also identified. This burden of disease within the antenatal and neonatal population highlights the need for effective screening during pregnancy and following delivery.

04. New developments in basic science

PD-634-27 Effect of aldehyde dehydrogenase 2 genetic polymorphism on human airway stem/progenitor cell function in vitro

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Background: Mutation in ALDH2 gene affects 40% of East Asians and causes complete loss of its enzymatic activity. People with this mutation have increased risk for many diseases and cancers. High levels of ALDH expression are observed in the stem/progenitor cells of many tissues and organs. The effect of the mutation on lung pathology is yet to be elucidated. The purpose of this in vitro research is: 1) to characterize the effect of ALDH2 disturbance on human airway stem/progenitor cells function in homeostasis and after injury, and 2) To examine the effect of pharmacological ALDH2 induction on stem/progenitor cells function.

Design: We used optimized enzyme digestion protocol to isolate primary human bronchial and distal lung epithelial cells from fresh surgical specimens while ALDH2 genotyping was tested by specific probes. Then basal and alveolar stem/progenitors were purified separately using fluorescence-activated cell sorting. In vitro sphere forming assays and immunofluorescence staining were performed to compare their self-renewal, differentiation capacity in both homeostasis and reactive oxygen species (ROS) injured circumstance between ALDH2 targeted polymorphism groups. Pharmacological interferences with ALDH2 activator were further evaluated.

Results: 15 ALDH2 wild type and 11 hetero-mutant human airway specimens were processed. The sphere forming efficiency (SFE) of ALDH2 wild type primary bronchial epithelial stem/progenitor cells (ES/PCs) was 3.13% and that of distal lung was 0.3%, higher than that of ALDH2 mutant with 1.58% and 0.12% separately. However, there was no statistically significant for their SFE between the two polymorphism groups. Airway stem/progenitor cells with different ALDH2 genotypes presented similar differentiation profiles. Exposed to ROS injury, airway ES/PCs with ALDH2 mutation presented higher SFE than that of wild type. Treated with ALDH2 activator Alda-1, both wild type and ALDH2 mutant airway ES/PCs showed increased SFE. No significant effect was found on differentiation capacity with Alda-1 or ROS treatment between varied ALDH2 genotyping groups.

Conclusions: ALDH2 mutation presented little detectable functional impairment in human airway stem/progenitor cells in homeostasis. Potential mechanism of injury induced self-renewal improvement with ALDH2 mutation needs to be explored.

PD-635-27 Pre-exposure to household air pollution dampens human alveolar macrophage responses during *Mycobacterium tuberculosis* infection

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Background: Household air pollution (HAP) affects 3 billion people due to domestic burning of solid fuels. The global burden of tuberculosis (TB) is greatest in poor countries where HAP exposure is highest. Systematic meta-analyses have described associations between HAP and TB, but pathophysiological mechanisms underlying these are uncertain. HAP particulates and *Mycobacterium tuberculosis* share similar HAM response pathways. Chronic particulate exposure also dampens macrophage responses. Here, we use an ex vivo model to generate pilot data on interactions between carbon-exposed human alveolar macrophages (HAMs) and *M. tuberculosis*.

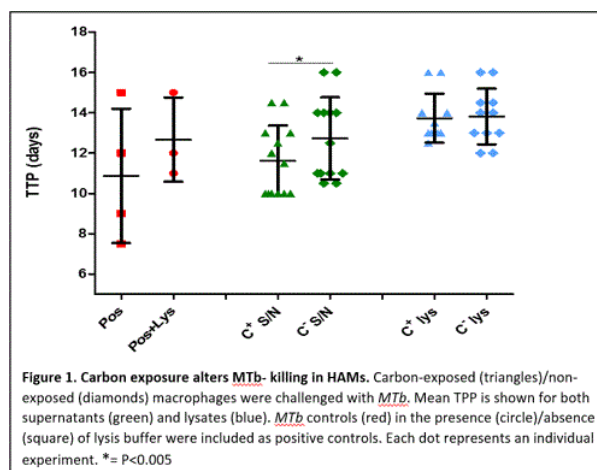
Methods: HAMs were obtained from bronchoalveolar lavage (BAL) of 6 healthy volunteers, exposed to ultra-fine carbon, and then incubated with *M. tuberculosis*. The capacity of HAMs to control *M. tuberculosis* infection was assessed by liquid (MGIT) and solid (Middlebrook 7H11) culture supernatants and cell lysates. Time to positivity (TTP) and colony counts were used to quantify extracellular (supernatant) and intracellular (lysate) bacillary load.

Results: The Figure shows that supernatant from carbon-exposed HAMs had shorter liquid culture TTP, thus higher *M. tuberculosis* load, than non-carbon-exposed control cells (mean = 11.6 days [SD = 1.8] vs. mean = 12.7 days [SD = 2.0]). This difference was not observed from solid media colony counts. Lysis buffer diminished

M. tuberculosis viability. No effect of carbon exposure was detected from inoculation of cell lysate with either culture media.

Conclusions: 1) Shorter TTP in MGIT culture of supernatants following carbon-exposure suggests that carbon dampens macrophage responses to extracellular bacteria. 2) Non-observation of this effect in solid culture, may reflect varying properties of different media to quantify *M. tuberculosis* growth. 3) Lysis buffer reduces *M. tuberculosis* viability in cell lysates, potentially obscuring the effect of carbon on intracellular organisms. 4) These pilot data suggest that innate immunity in patients with pulmonary tuberculosis is compromised by particulate exposure. Our translational approach of studying HAMs from volunteer BALs may help explain this.

Figure Carbon-exposure dampens extracellular HAM response



PD-637-27 Comparative study of *Piper nigrum*, *Piper album* and *Piper longum* on various characteristics of pyrazinamide and ethambutol microspheres

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Background: Bioenhancers are chemical entities used to promote and augment the bioavailability of the drugs which are mixed with them and do not exhibit synergistic effect with the drug. The need for bioenhancers arises due to drugs which are poorly available, administered for long periods, toxic and expensive. In a cited research work, the effect of various species of piper viz. *Piper nigrum*, *Piper album* and *Piper longum* used singly and in combination in an equal ratio. The in vitro release and other characteristics of most commonly used first line

anti-tubercular agent Pyrazinamide and Ethambutol formulated as microspheres are studied.

Methods: Complex Coacervation and Modified Emulsion Method were used to prepare microspheres.

Material: Pyrazinamide, Ethambutol, *Piper nigrum*, *Piper album* and *Piper longum*.

Results: The in vitro drug release of Pyrazinamide and Ethambutol from formulations where *Piper nigrum* was used as bioenhancer was found to be about 66–70% in 12 hrs, when single bioenhancers were used. In case of bioenhancers used in combination the in vitro drug release of Pyrazinamide and Ethambutol was increased up to 85–90% for combination of *Piper nigrum* and *Piper longum* in a equal proportion, the same was about 35–40% in case of formulations where no bioenhancer was used. Other parameters like percentage bioadhesion, permeability study using intestinal sac method etc. were also studied.

Conclusions: The microspheres prepared by both complex coacervation and modified emulsion methods; the particle size was uniform and found to be less than 130 micron in size. The drug encapsulation efficiency was found to be in the range of 27–67%. The percentage bioadhesion of the microsphere were found to be 20–76% (were significantly increased in the formulations where bioenhancer were incorporated). The in vitro release study by USP paddle apparatus and the most important results from the in vitro release study relates to the very significant enhancement in drug release (40 to 90% for microspheres prepared by modified emulsion method and 35 to 85% complex coacervation method), due to presence of bioenhancer.

PD-638-27 Increased growth due to overexpression of cholesterol import gene in *M. tuberculosis* H37Rv

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Background: Lipid synthesis forms the heart and soul of mycobacteria life cycle inside its host. The host cholesterol has been found to be an important source of carbon for *M. tuberculosis* and helps in prolonged survival. *mce4* operon in *M. tuberculosis* encodes for this cholesterol uptake system and it is also required for entry of mycobacteria into macrophages through cholesterol rich domains. Cholesterol is further catabolized by *M. tuberculosis* by two different pathways i.e. methyl citrate cycle (MCC) and methylmalonyl pathway (MMP). *mce4A* gene of *mce4* operon has previously been shown to have strong affinity for cholesterol and is involved in uptake of cholesterol. Through this study we demonstrate the role of *mce4A* in expression of MCC and MMP.

Methods: *mce4A* overexpressing *M. tuberculosis* H37Rv was used as the test recombinant strain and *mce4A* antisense *M. tuberculosis* H37Rv as the negative control.

Growth of recombinants and wild type *M. tuberculosis* H37Rv was monitored in the presence of cholesterol as sole source of carbon. Glycerol containing medium was used as the control set. Expression profile of MCC and MMP related genes was studied using RT-PCR and lipid accumulation was analyzed using thin layer chromatography.

Results: Increased growth of *mce4A* overexpressing *M. tuberculosis* H37Rv supported with increased expression of MCC in cholesterol as well as glycerol under different medium conditions explained the influence of *mce4A* on expression of MCC genes. Lipid elongation genes were significantly overexpressed in *mce4A* overexpressing *M. tuberculosis* H37Rv along with increased free lipid accumulation. *mce4A* antisense was unable to grow in cholesterol containing medium and demonstrated low expression level of MCC and MMP genes along with low free lipid accumulation.

Conclusions: Our study demonstrates that cholesterol import associated gene, *mce4A*, induces methylmalonyl pathway mediated free lipid synthesis. Utilization of cholesterol as the carbon source influences the methylcitrate and methylmalonyl pathway genes expression and growth of mycobacteria. This presents *mce4A* as an effective drug target which will help limit the entry of cholesterol as well as its utilization by mycobacteria, required for attaining dormant condition. Decrease or inhibition in lipid accumulation will also help in increased permeability of mycobacterial cell wall.

PD-639-27 Pharmacodynamic interaction assessment of anti-tuberculosis drugs in a pre-clinical setting

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Background: Effectively treating a tuberculosis patient involves using a combination of drugs. When combinations of different drugs are used the possibility of interactions resulting in deviations from the observed individual drug effect exists. For many reasons, optimizing the drug combinations and dosages is impossible perform to in a clinical setting without prior pre-clinical research. The presented work aimed at assessing the pharmacodynamic interactions of combinations of isoniazid, rifampicin and ethambutol using in vitro time kill data.

Methods: In vitro time kill experiments¹ were performed with *M. tuberculosis* genotype strain Beijing-1585 using both single and combination series of rifampicin, isoniazid and ethambutol concentrations. Viability, defined as colony forming units (cfu), was assessed at day 1, 2, 3 and 6 after drug exposure. The Multistate Tuberculosis Pharmacometric (MTP) model framework² and the general pharmacodynamic interaction (GPDI) model based on the Bliss Independence criterion³ was used to characterize drug effect from mono and

combination exposure using nonlinear mixed effects methods.

Results: A pharmacological antagonistic pharmacodynamic interaction was found between rifampicin and isoniazid with a larger antagonistic effect on isoniazid by rifampicin than vice versa. An antagonistic interaction was found between isoniazid and ethambutol, but the interaction effects were similar between the two drugs and the maximum fractional increase in EC_{50} of < 1 was similar to that of the antagonistic interaction between ethambutol and rifampicin. In contrast, a synergistic interaction was found between rifampicin and ethambutol and there was no significant difference in the size of synergy exerted by rifampicin on ethambutol and vice versa.

Conclusions: We have in this work shown how an assessment of pharmacodynamic interactions can be carried out using the MTP model together with the newly developed GPDI model. This work represents a first step towards a complete characterization of the in vitro pharmacodynamic interactions between the current anti-tuberculosis drugs thus providing groundwork for evaluation of new and optimization of current drug regimens.

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PD-640-27 Assessment of pharmacodynamic interactions in tuberculosis infected mice using the Multistate Tuberculosis Pharmacometric Model and the General Pharmacodynamic Interaction Model

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Background: Precision medicine and knowledge on understanding anti-tuberculosis drug pharmacodynamics (PD) interaction are essential in clinical settings as well as drug developments. Mouse model could provide useful information on drug efficacy before entering clinical trials. The aim of this work was to investigate PD interactions between anti-tuberculosis drugs in an chronic TB mouse model using the Multistate Tuberculosis Pharmacometric (MTP) model and the general pharmacodynamic interaction (GPDI) model based on the Bliss Independence criterion.

Methods: Pharmacokinetic (PK) models for rifampicin (RIF), isoniazid (INH), pyrazinamide (PZA) and ethambutol (EMB) were developed using sparse and rich observations from infected and healthy BALB/c mice, respectively. Infected mice randomized to monotherapy received 4 weeks of RIF (5, 10 or 20 mg/kg) or INH

(12.5, 25 or 50 mg/kg) or EMB (50, 100 or 200 mg/kg) or PZA (75, 150 or 300 mg/kg). Colony forming unit (cfu) was measured after 1, 2 and 4 weeks treatment using 9 mice at each occasion. In duo, triple and quarto combinations, fixed doses of RIF (10), INH (25), EMB (100) and PZA (150) were used and cfu was measured after 1, 2, 4, 8, 12 and 24 weeks of treatment using 3 mice at each occasion. Natural growth data was collected at 1, 3, 7, 14 and 21 days after infection.

Results: In monotherapy, RIF killed fast- (F), slow- (S) and non-multiplying (N) bacteria as well as inhibit the growth of F bacteria. INH had no effect on N, but killed F and S bacteria. EMB and PZA displayed no killing effects, because of lack of longitudinal cfu data. In the presence of PZA, INH killed N bacteria. Compare to expected additivity, antagonism was quantified between RIF and INH against S and N bacteria, which increased 0.79 and 0.86 log₁₀ cfu. EMB synergized RIF on killing N bacteria, which decreased 2.84 log₁₀ cfu.

Conclusions: This study suggests that the MTP model together with the GPDI model can be applied to both mono and combination therapies cfu data from animal studies, which provides a quantitative evaluation framework of potential PD interactions among anti-tuberculosis drugs in drug development.

PD-641-27 Antipyrene derivatives in the treatment of tuberculosis

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Background: TB is a major public health problem in many low and middle income countries, where the number of people with diabetes is also rising rapidly. Regions, such as Africa and Asia that are most heavily affected by tuberculosis are also those that have some of the highest numbers of people with diabetes and will experience the biggest increases by 2030. Most of the anti-tubercular agents are hetero-aromatic compounds like isoniazide, nitroaromatic compounds, thiazine, benzothiazole, etc. Antipyrene is also a heterocyclic compound which has been drawn as promising structural unit in the field of medicinal chemistry. It is already reported having potent insecticidal,¹ antimicrobial, anti-tumor and anti-inflammatory² activities etc.

Methods: The present work deals with the synthesis and evaluation of biological activities of 4-aminoantipyrene derivatives derived from different aromatic acids. The synthesis is completed with amide bond formation having 92–95% yield. The structures of synthesized derivatives were established on the basis of spectroscopic and elemental analysis.

Results: All derivatives have screened for anti-tubercular activity. The screening results have shown that compounds most of them having moderate to good anti-tubercular activity. Some of them are in process of biological evaluation for IC₅₀ value.

Conclusions: The bioactivity of these derivatives has also been evaluated with respect to Lipinski's rule of five using mol-inspiration and chem-informatics softwares.

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PD-642-27 A novel therapeutic vaccine against tuberculosis in the cynomolgus monkey model: preclinical study and clinical trial

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Background: Multidrug-resistant (MDR), especially extremely drug resistant (XDR), *Mycobacterium tuberculosis* is a big problem in the world. We have developed a novel TB therapeutic vaccine (HVJ-E/HSP65 DNA +IL-12 DNA vaccine) to eliminate MDR-TB.

Methods: DNA vaccine expressing TB heat shock protein 65 and IL-12 was delivered by the hemagglutinating virus of Japan (HVJ)-envelope. Human *M. tuberculosis* was intratracheally instilled into cynomolgus monkeys and then the monkeys were treated with the vaccine i.m.

Results: This vaccine provided remarkable protective efficacy compared to BCG vaccine and strong therapeutic efficacy against MDR-TB and XDR-TB in murine models. This vaccine induced strong CTL against TB and production of IFN- γ , while BCG vaccine induced little CTL. Furthermore, this vaccine provided therapeutic efficacy of prolongation of survival time of TB infected monkeys and augmented the immune responses (the augmentation of IL-2 production and the proliferation of PBL of monkeys). Therefore, the preclinical tests were studied in GLP level. The injection of 100 μ g of the vaccine /mouse i.m. three times in two weeks was optimal for the production of IFN- γ and IL-2. By the toxicology test using monkeys, high dose 4.5mg GMP level vaccine/monkey(kg) showed little toxicity (hematology, blood chemistry). Safety pharmacological study of repeated administration showed safety against central nervous system. By the toxicokinetic (TK) test of human IL-12 in the blood of monkeys immunized with the vaccine, little human IL-12 was observed. Furthermore, we have planned to do clinical Phase I trial. Targets are human patients with MDR-TB. The safety and tolerability of the vaccine will be evaluated.

Conclusions: These data indicate that our novel vaccine might be useful against tuberculosis including XDR-TB and MDR-TB for human therapeutic clinical applications.

Co-workers: K Tomono, A Kumanogoh, S Syoji, A Mikami, T Saito, T Matsumoto, S Hayashi, D McMurray, E Tan

PD-643-27 Observational study of the duration of protection of school age BCG vaccination in England

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Background: Long term follow-up of a BCG vaccine trial in North American Indians suggested BCG vaccination protects against TB for several decades. A cohort study in Brazil and more recently in Norway also suggest protection lasts for more than one or two decades. Establishing duration of protection is of relevance given disease risk is higher in young adults and the proportion pulmonary disease, the main source of onward transmission, increases with age. We took advantage of the UK's universal school-aged BCG vaccination programme to examine long term protection against TB.

Methods: We carried out an observational study in England of cases of tuberculosis and frequency-matched population-based controls in the UK born white population offered BCG vaccination 10 to 30 years earlier. We studied vaccine effectiveness (VE) as a function of time-since vaccination using a case-cohort analysis based on Cox regression for most efficient use of controls. We also examined confounding by socio-economic and more proximal factors such as smoking, drug use, prison and homelessness.

Results: Based on a 60% response rate in both cases and controls we recruited 677 and 1170 subjects respectively. After stratifying by birth cohort and adjusting for sex, VE was better in the first 20 years after vaccination than after 20 years. Area based levels of deprivation and education level only were noted as confounders, but changed VE estimates only slightly. Adjusted VEs (95%CI) were 58% (36–73%) 10–15 years after vaccination, 61% (42–74%) 15–20 years and 36% (8–55%) 20–25 years after vaccination. Numbers were too small to provide more than borderline evidence of low protection at 25–30 years (adjVE 23% (0–55%).

Conclusions: The evidence from a general population study in England supports the suggestion in the Norwegian study that protection by BCG against TB lasts for at least 20 years after school aged vaccination and continues at a lower level after. The findings may be useful for decisions on TB vaccine programmes (eg timing of new vaccines) and for cost effectiveness studies. Assessment of new vaccines will also need to show they offer protection against TB greater than that offered by BCG alone.

PD-644-27 ICAM-1: a potential link between tuberculosis and type 2 diabetes mellitus

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Background: It is a well-known fact that type 2 diabetes mellitus (T2DM) makes a substantial contribution to tuberculosis incidence. The huge prevalence of diabetes mellitus in Pakistan may be contributing to the increasing prevalence of TB incidences. The objective of the present study is to evaluate the role of sICAM-1 as a potential link between these two merging epidemics.

Methods: To explore this hypothesis three groups of subjects were examined: 100 healthy controls, 100 T2DM patients and 100 patients with T2DM and TB. As leukocyte integrins such as ICAM-1 have a significant effect on the functions of macrophages, so various hematological parameters such as WBCs, RBCs, Lymphocytes, Neutrophils, Platelets, Hemoglobin were also measured. In vivo production of sICAM-1 was measured using ELISA.

Results: When compared with healthy controls, patients with T2DM were found to have elevated levels of sICAM-1 ($541.8 \text{ ng/ml} \pm 5.2$; $P < 0.05$), patients with T2DM and TB were found to have low levels of sICAM-1 ($127.7 \text{ ng/ml} \pm 4.1$; $P < 0.05$). Our data suggested that in T2DM patients, elevated ICAM-1 levels are also responsible for reduced functioning of endothelial cell barriers. Thus in diabetic patients increased expression of sICAM-1 make them prone to infectious diseases such as tuberculosis by promoting increased invasion of mycobacterium through loose junctions. Moreover decreased cellular immunity in diabetic patients further worsens the condition. All these dysfunctional processes put diabetic patients at increased risk of tuberculosis.

Conclusion: In conclusion, present study demonstrates that elevated levels of sICAM-1 can be used as a biomarker to predict tuberculosis in patients with type 2 diabetes mellitus.

05. 'Help!': no drugs, no programme

PD-645-27 Implementation of digital health tools facilitates strategic information for decision making on TB pharmaceutical management in Tajikistan

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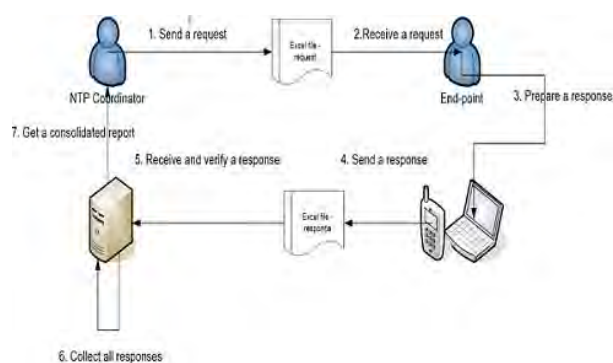
Background and challenges to implementation: Tajikistan is among the 30 high burden MDR-TB countries. Among several factors for high MDR-TB rates, inadequate TB pharmaceutical management (PMTB) holds one of the leading positions. The paper-based TB logistics

management information system (LMIS) is well designed but requires lots of efforts and time from the National PMTB coordinator to ensure quality data collection. Hence, it is not sufficient for promoting strategic information for decision making, hindering the desire for uninterrupted TB-medicines supply for patients.

Intervention: In regards to increase use of information for decision-making in TB-medicines regular supply planning at different levels of the TB network, the US Agency for International Development (USAID)-funded Systems for Improved Access to Pharmaceuticals and Services (SIAPS) Program provided technical assistance to the National TB Program and developed a downloadable desktop tool VSPMIS (Very Simple Pharmaceutical Management Information System), which allows to aggregate and analyze LMIS data, monitor metrics like reporting rates, average monthly consumption, and thus manage stock levels to minimize expiries and stock-outs. The tool passed a six month of intensive testing mode at country level and the responsible staff in e-reporting were trained. A system for reporting was designed which is presented in the figure below:

Results and lessons learnt: During the first half of 2016, e-reporting and VSPMIS is being piloted at 6 districts of Tajikistan in conjunction with other international partners and expected to start rollout throughout the country by the end of year.

Conclusions and key recommendations: Partner organization should support the NTP in e-reporting and VSPMIS implementation, because with the existing information load, nowadays, electronic reporting along with the tools which is capable to transform complicated calculations into the ready spreadsheets displaying key information for managing medicines, becomes an essential element in PMTB and thus of the overall national TB programs.



PD-646-27 Interventions for program implementation of bedaquiline in Georgia

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Background: Program management of drug-resistant Tuberculosis (DR-TB) remains one of the main challeng-

es for the Georgian Public health system. In 2012, DR-TB was found in 9.2% of new TB cases and 31.2% of re-treatment cases, while in 2014, in 11.6% and 39.2% respectively. Successful treatment outcome with second line anti-TB drugs was only 41% in 2013 cohort. The severity of the problem has necessitated the implementation of the new DR-TB treatment program as a part of the National TB Strategic Plan 2016-2020 based on the End TB Strategy.

Interventions: Introduction of Bedaquiline (Bdq) through a compassionate use program (CU) started in Georgia in 2011 and from 30 July 2014 continued in the framework of the new DR-TB treatment program with the support of MSF-France. Georgia developed a National Bedaquiline Implementation Plan based on the latest recommendations of the WHO. To decentralize the DR-TB patients' enrollment in new regimens and to monitor the treatment implementation, an innovative approach of 'Mobile Consilium' was elaborated. Early adoption of the new treatment regimen made Georgia a primary candidate to receive free courses of Bdq through the USAID and Janssen Therapeutics Bdq Donation Program in July of 2015 for program use.

Results: From 2011 to July, 2014, 12 patients were enrolled in the CU program. All of them finished the course with successful outcome. From 30 July 2014 to 1 March 2016, 204 patients were discussed countrywide for the new program and 176 started the treatment with Bdq, including 14 patients from the penitential system. Each patient's enrollment, monitoring and supervision are accomplished by the Central DR-TB Committee and 'Mobile Consilium'. The milestones for the effective introduction of the new drugs as a part of combination therapy were: updating of National TB Guidelines, increasing Laboratory Capacity by universal access to first and second line Drug Susceptibility Testing including the rapid molecular tests (HAIN MTB-DR^{Plus}/sl and Xpert MTB/RIF), creation of Pharmacovigilance Committee, training courses for TB-doctors from all regions of the country.

Conclusion: Program administration of the new DR-TB treatment regimens in line with the active drug safety monitoring seems to have promising effects on the epidemiological situation in Georgia.

PD-647-27 Improving the management of tuberculosis and leprosy medicines through an optimized logistics system: the experience of Tanzania

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Background and challenges to implementation: Existence of a well-coordinated TB supply chain system from central to health facility (HF) level is critical in order to avoid TB treatment interruptions. In 2011, the National

TB and Leprosy Program in collaboration with the Supply Chain Management System (SCMS) project implemented by John Snow Inc. (JSI) conducted an assessment which highlighted a number of challenges that affect management of TB and Leprosy (TBL) medicines in Tanzania. These include a lack of standardized methods for resupply of medicines to districts and health facilities, nonexistence of standardized logistic management Information tools (LMIS), unavailability of standardized procedures for filling LMIS tools, varied frequency of distribution of medicines from the district to the facilities, limited data visibility and expiries of medicines

Intervention or response: To address these challenges, NTLP in collaboration with SCMS redesigned the TB logistics system and integrated the reporting and ordering of TBL medicines into the electronic Logistics Management System (eLMIS). This aimed at establishing a standardized system for regular supply of TBL medicines; improve data visibility and quality of data for decision making. The optimized system was piloted in few districts followed by a countrywide roll out.

Results and lessons learnt: The capacity of 3877 health workers to use the optimized system has been enhanced covering 165 districts. Standard resupply system for TBL medicines is now operational. Facilities are currently able to report on TB stocks on hand and the number of patients currently on treatment to the district on monthly basis. This has helped to ensure evidence based decision making at districts level hence improved resupply to HFs and redistribution within the districts. The system has also reduced delays in delivering TBL medicines to the districts and health facilities through harmonizing the distribution with other health commodities.

Conclusions and key recommendations: The implementation of the optimized system has demonstrated dependability and ensured coordinated proper management of TBL medicines. However for its efficiency, there is a need to maintain adequate TB stocks at the central level to ensure that order fill rates are high. Moreover, we recommend that on going monitoring and capacity building of health care workers is important.

PD-648-27 Sustainable engagement of pharmacists in TB care and control: experiences from the PRATAM Project, India

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Background and challenges to implementation: Pharmacists can play a very vital role in TB care and control being first avenues for any sort of treatment. But wide spread belief is that they are too busy and business oriented to support a social cause. TB Alert India has taken up a project engaging Pharmacists in TB Care and Control with financial support from Lilly MDR-TB Partnership. Project is being implemented since 2012 in Telangana state, India. From Feb 2013 to Sept 2015, 175 pharmacists facilitated testing of 2940 people with TB

like symptoms. Around 11% (329/2940) are diagnosed with TB. Analysis of project MIS was taken up to understand the pattern of pharmacist's involvement across three years. Objective was to understand whether project initiatives will sustain after project closure.

Intervention or response: After sensitization and training pharmacists are enrolled in the project and unique ID is allotted. Performance of individual pharmacist is tracked in the extensive project management information system (MIS). Data from Sept 2012 to September 2015 was analyzed for two basic indicators: 1) How many of the enrolled pharmacists year wise are still involved with the project, and 2) What are the referral trends across the years by pharmacists?

Results and lessons learnt: Findings of the analysis are really encouraging. Around 101 trained pharmacists in year 1 facilitated testing of 547 people with TB symptoms in year 1. Around 13% (72/547) were diagnosed with TB. In year 2 and year 3 number of people tested due to pharmacists increased to 640 and 746 respectively by these pharmacists. Around 11% were diagnosed with TB in both years (72/640 and 82/746). Similarly around 74 new pharmacist trained in year 2 facilitated testing of 261 and 439 in year 2 and year 3 respectively. Around 7% (18) and 10% (439) are diagnosed with TB in year 2 and year 3, respectively. Results indicate that pharmacists are showing interest and getting engaged with NTP.

Conclusions and key recommendations: Pharmacists engagement could be successful and sustainable which are yet to be explored in full.

PD-649-27 An analysis of supply chain management policies to reduce stockouts of drugs for MDR-TB

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Background: Stockouts of second-line anti-tuberculosis drugs (SLDs) lead to treatment interruption which can force changes in patient drug regimens, drive drug resistance and increase mortality. Though the literature proposes improvements to the global SLD supply chain policies, there is limited quantitative modelling that accurately predicts the expected impact of these proposed changes on the availability of SLDs.

Methods: This study focuses on the downstream component of the global SLD supply chain, modelling the supply of amikacin in the Western Cape province in South Africa using a system dynamics simulation approach. The model is used to 1) implement a Supply Chain Operation Reference framework-based analysis of the key performance indicators of reliability, responsiveness and agility; and 2) impact evaluation of proposed changes to the operation of the downstream supply chain: improved inventory management, demand fore-

casting and public tendering. The model uses data for the period 2004–2014 for 1) orders placed to, and received from, all suppliers to the centralized provincial drug depot (Cape Medical Depot, CMD), and 2) orders placed to and received from the CMD by 345 healthcare facilities.

Results: The CMD stocks 267% more units of amikacin than required on average every month, indicating sub-optimal inventory management. An analysis of 121 scenarios for changes to the operation of the supply chain indicate that inventory management approaches can cost-effectively reduce stock-outs of SLDs. Specifically, determining safety stock levels based on the percentage increase in demand between months, whilst incorporating static minimum and maximum desired stock levels, produces pareto optimal results. Reducing supplier lead-time, and implementing an exponential smoothing forecasting technique, also reduces the likelihood of stockouts.

Conclusions: The results support the recommendations for operational changes proposed in the literature. We produce concrete, actionable guidelines, that are within the control of governmental medical depots, to cost-effectively reduce stockouts.

PD-650-27 Benefits of implementing an early warning system to improve decision making in five African countries

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Background and challenges to implementation: Ensuring that patients have continuous access to tuberculosis (TB) treatment requires accurate projections of TB medicines needs by TB program staff and other key stakeholders. The process becomes more challenging as new diagnostic tools are rapidly introduced leading to anticipated increase in the number of TB patients and quantities of TB medicines needed. However, limited capacity to estimate TB medicines needs and regularly monitor TB stock status are some of the key challenges contributing to frequent stock outs and wastage of TB medicines in many African countries.

Intervention or response: To meet the changing needs of the expanding programs, from 2013, USAID funded Systems for Improved Access to Pharmaceuticals and Services (SIAPS) program supported National TB Programs (NTPs) to achieve uninterrupted supply of TB medicines. SIAPS supported countries to establish a sustainable system which provides early alerts about supply chain problems such as stock-outs or expiries for quick, evidence based decisions and actions to mitigate them. For this system to work well, countries are required to collect relevant data and monitor TB medicine stock status on quarterly basis.

Results and lessons learnt: All five countries were able to improve their TB supply chain practices as a result of this

intervention. Stocks-outs of TB medicines reduced ranging from 38% to 0% for first line TB medicines and from 17% to 0% for second line medicines. Where medicines were overstocked, postponement of pending shipments helped save over 4.7 million USD which could potentially expire if received in the countries. Cross border transfer of excess stocks which were at risk of expiring contributed to over 1.4 million USD in savings. Besides improvement of TB medicine forecasting, supply planning and procurement practices; data from this system also highlighted weaknesses in TB patient management, TB recording and reporting practices and inventory management.

Conclusions and key recommendations: Effective and regular monitoring of TB stock levels against patient enrollment is key to ensure early identification of potential TB medicines wastage or stock outs. However, more efforts need to be made to address other factors contributing to overstocks or stock outs of TB medicines.

PD-651-27 Private pharmacists: a vital link in the PPM model for TB control in Chennai city, India

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Background and challenges to implementation: Private pharmacists are a critical but often ignored component in any private health sector involvement for TB control, because they are closest to the community and are hence also in a position to influence patients' treatment choices. Chennai city, with a 4.7 million population, has a presence of huge and vibrant private health sector and pharmacies.

Intervention: 1) A sustainable partnership for TB control with private pharmacists. 2) To facilitate early diagnosis of TB patients by encouraging referrals from private pharmacists to public/PPM (Public Private Mix) centers. 3) To engage the pharmacists in referring TB patients for free treatment provided under RNTCP (Revised National Tuberculosis Control Program); 4) To involve pharmacists as community DOT (Direct Observed Treatment) providers. 5) To promote awareness on TB and cough hygiene by the private pharmacies.

Results: Of the 1096 pharmacists trained from January 2013 to December 2015, one third of them referred 1179 presumptive TB patients. Of the 1179 referrals, 757 (64%) referrals were to PPM centers and the remaining to the public health centers. Of the 792 presumptive TB patients, 482 underwent diagnosis and 127 (26%) were diagnosed with TB. Of the 438 TB patients referred from the pharmacists, 195 were started on treatment under RNTCP. In all, 291 TB patients received treatment under RNTCP and 185 TB patients on treatment in private sector received education and information on TB. About 116 pharmacists were DOT providers to 190 TB patients. Qualitative data findings from patients revealed that they found it very convenient to receive DOT from pharmacists.

Conclusion: The above finding has shown that pharmacists could be successfully engaged in TB control efforts. In addition, the pharmacists had educated patients by displaying posters, directing them to appropriate treatment choices and by motivating patients for completion of the treatment course. The finding has reiterated the need to look at all stakeholders in the private health sector. The contribution of private pharmacists towards DOTS program could be considerable and it is critical to engage with them in a sustained manner.

PD-652-27 Uzbekistan's new approach to tackle the MDR-TB burden through an institutionalized early warning and quantification system

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Background and challenges to implementation: When a comprehensive indicator-based assessment of Uzbekistan's tuberculosis (TB) pharmaceutical system was conducted in 2014, findings revealed gaps in the number of contributing factors for the prevailing high rates of MDR-TB including inadequate supply planning for medicines. Out of 28 visited warehouses, 20 (71%), reported stock-outs of TB medicines for last 12 months. Nine of those warehouses, (45%) reported that the main reason for stock-outs was incorrect forecasting and quantification.

Intervention: To avoid problems with stocks-outs, in February 2015, we piloted an early warning and quantification and forecasting system (EWS) with the use of QuanTB - a downloadable desktop tool that transforms complicated calculations into a user-friendly dashboard displaying key information for managing medicines in four regions of country. The patient and stock related data flow and reporting system was designed and tools for data collection was developed. Nineteen responsible staff at the regional and national levels were trained and regular monitoring visits were established. Regional TB facilities representing an intermediate level of the NTP were requested to perform quantification using QuanTB for entire region on monthly bases and report to the central level.

Results and lessons learnt: In three out of 4 pilot regions, the EWS was regularly used for TB medicines ordering for the regional and district levels, which ensured good coordination between the central and regional levels to assure that optimal level of stocks are maintained at all TB facilities. Based on the lessons learnt and results of the pilot, the EWS began nationwide implementation with capacity built in all 14 regions. The Ministry of Health issued an order obliging all regional TB facilities using EWS for regular TB medicines ordering and providing

QuanTB summary tables to the central level for further data aggregation and analyses.

Conclusions and key recommendations: EWS is an important element for supply planning of TB medicines at different levels of the system. However, the EWS element alone cannot ensure uninterrupted supply of medicines if other elements of supply chain, like distribution system, warehousing and transportation are not concomitantly addressed.

PD-653-27 Aligning TB control activities to the devolved system of governance in Kenya

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Background: After the adoption of a new constitution, Kenya devolved all aspects of health care services to the 47 newly created counties. Before devolution, TB control activities were being managed from national level with 12 control regions directly reporting to the central unit. One of the consequences of devolution in TB control in Kenya was severe shortage of TB drugs experienced in 2014 since neither the counties nor the national government budgeted for procurement of the same resulting in drugs being borrowed from Malawi. To ensure proper coordination of TB control activities under devolved system, there was need for the national TB control program to realign with the system.

Methods: In 2014, the National TB, Leprosy and Lung Disease Program (NTLDP) held 2 consultative forums with county health managers from all the 47 counties to discuss and agree on how to effectively work together. The forums discussed coordination between the two levels of government, and commitment of counties to TB control. The NTLDP also continuously engaged the counties to ensure deployment of qualified officers and the electronic surveillance system was also modified to be able to provide data both at the national and county levels.

Results: As at February 2016, all the 47 counties had appointed County TB and Leprosy Coordinators while the number of TB control zone coordinators had risen from 257 in 2013 to 285. The counties have been organized into 17 clusters for ease of coordination and facilitation of quarterly data review meetings based on county proximity to each other and similarities in TB burden. The clusters have held 7 quarterly meetings with the attendance of county health directors. Four technical assistance missions have been held jointly between counties and the national program as well as two data quality assessment missions. Counties have access to their county specific TB data.

Conclusion: Efforts made by NTLDP to align TB control to the devolved system have borne fruits. There are still aspects that counties need to take up including facilitating sub county coordinators to conduct routine support

supervision, provision of tools, and support of the electronic surveillance system

06. Raising TB awareness

PD-654-27 Engaging Laskar TB Remaja (The Youth TB Warriors) in Depok City, Indonesia: a new hope in enhancing TB awareness

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Background: Indonesia still faces enormous challenges in TB control. As future leaders, the youth should be introduced early on TB disease to take active roles. Since young people are more open to receive information, peer group approach could potentially be more easily acceptable among them and become a new strategy. Indonesian Association Against TB (PPTI) has initiated special efforts on the youth segment through *Laskar TB Remaja* (The Youth TB Warriors).

Intervention: In cooperation with the district government, district health and education officers, PPTI Depok has conducted recruitment events among junior and high school students, college students, youth organizations, and scouts. Advocacy meetings with members have performed to facilitate capacity building on TB, as well as communication skills. They have become peer educator cadres.

Results: In the beginning of 2015, 250 youth were recruited as Laskar TB Remaja. Along with increasing TB knowledge, they have become more confident in sharing and providing education to their peers. With the support of various parties, a lot of innovation activities has been carried out: 'TB troops go to school/campus' which has included 700 students, TB awareness promoting at 3 shopping malls, making media education both printed and electronic, held various activities to commemorate The World TB Day 2015: 'Walk for TB', media outreach competition, quiz competitions, musical and art performances, which have involved nearly 1,000 participants. They have also conducted 4 times jamboree (outdoor meetings) involving 500 participants, and participating to capture TB suspects at their schools and communities. Involving teachers in the implementation of Laskar TB Remaja program was also conducted. Almost all participants prefer to receive information and discuss it with peers. Whilst one of the biggest challenges is the limited financial resources and facilities, but similar activities should be promoted in other areas. It could become a new strategy in campaigning better TB control, considering the youth segment occupies a large part of Indonesian population.

Conclusions: Efforts to engage the youth participation in TB control is very important as they are able to communicate and convey information better with peers. It could become a new hope in increasing TB awareness.

PD-655-27 Effectiveness of a door-to-door outreach strategy on pulmonary TB detection in two health zones in Kinshasa, DRC

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Background: The Democratic Republic of Congo is ranked among the 22 countries with high burden of TB in the world. Despite efforts by the PNLTL, a third of patients expected in the country is still not reported and to this is added a dwindling of the notification of cases in the country (4% from 2010 to 2011). The Challenge TB project examined two health zones with low TB detection to assess the effectiveness the door to door outreach strategy on pulmonary TB detection and the use of rapid sputum diagnosis and integrating tuberculosis and HIV services within the community.

Methods: A mini awareness campaign was organized by the support of the Challenge TB project in April 2015 in two crowded health zones (HZ) that have always presented a low detection TB on the outskirts of Kinshasa (HZ Mont Ngfula1 and HZ Kinseso). During this campaign the samples of the suspects have been collected at the time of visited door to door in households by community volunteers briefed on the identification of suspect's concepts.

Results: After four days of campaigning in households door to door, 1634 households were visited and 2122 sputum samples collected from 1061 people suspected TB encountered. After analyzing the samples to the laboratory, 16 new (SS+) confirmed pulmonary TB patients were confirmed, tested negative for HIV and put on TB treatment against 7 cases detected each year on average in the two health zones. 69% were females and 62.4% were between 25–44 years of age.

Conclusions: Wide implementation of door to door outreach strategy, particularly in mini awareness campaign, should be optimized for active TB and TB-HIV case finding in DRC.

PD-656-27 Comparison of awareness about mode of TB transmission among the general population in 2011 and in 2013

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Background: Advocacy, communication and social mobilization (ACSM) as a strategy for TB control has been viewed with concern by TB experts due to

limitations in assessing the impact. In order to substantiate the progress of Axshya in achieving its objectives. A series of Knowledge, Attitude and Practice (KAP) surveys have been conducted at different time points under the project AXSHYA. The baseline KAP survey was conducted in 2010–2011. The midline survey was conducted between November 2012 and April 2013. The information generated through these surveys is representative of the various demographic and social characteristics of population living in these districts, keeping in view the relationship between these characteristics to tuberculosis control, and the impact of activities under Axshya.

Method: A cross-sectional community-based survey was conducted in 30 districts. the 30 districts were selected by a stratified cluster sampling technique out of the 374 project districts. Districts were initially stratified into the four RNTCP zones (north, south, east and west) of the country.

Results: A large percentage of the respondents were aware of the mode of TB transmission through air. This awareness was more than 65% across all zones. More than 40% of the respondents in north, east and west zones thought that sharing food with a person with TB can transmit TB. One fifth also responded that TB is transmitted through sharing bed or clothes used by TB patients. 14% of the respondents did not know the mode of transmission of TB at all. Although, there has been increase in the awareness level of the population on mode of transmission of TB.

Conclusion: The awareness on the mode of transmission among the general population is crucial to prevent TB transmission to family members and the community. This misconception would contribute to increase stigma and discrimination towards TB patients.

PD-657-27 Government and community challenge obstacles and create a model of high compliance with legislation in Tehri, a difficult hilly terrain

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Background: Indian tobacco control legislation (COT-PA-2003) prohibits smoking in public places. The law mandates that a specific signage informs people about smoke free status of a public place must be displayed at prominent places. Under the law, violators of the smoke free provisions will be fined up to INR 200. Tehri (population 616,409), a hilly district of Indian state of Uttarakhand, implemented various steps for enforcing smoke free legislation through massive awareness activities, series of capacity building programmes followed by effective law enforcement. This study conducted with an objective to assess the current level of compliance to the smoke free provisions of the law.

Methods: Smokefree compliance surveys are important tools to validate levels of compliance. An unobtrusive

cross sectional survey of randomly selected 405 public places in nine administrative blocks of Tehri district was done in the month of March 2015 by trained investigators using pretested checklist. The five core parameters of evaluation were: Presence of signage, absence of active smoking, absence of smoking aids, absence of tobacco litter and absence of tobacco smell.

Results: The 'No smoking signage' informing general public and tourists about smoke free provisions were observed at 86 % of public places; While 95% of public places were found without active smoking. 96.2% public places were observed free from smoking aids like ashtrays, match boxes & lighters. More than 91% of sampled public places didn't have any tobacco litter (cigarette butts and bidi ends). Over 95% of public places didn't have evidence of recent smoking as evident of absence of tobacco smell.

Conclusions: Tehri district has achieved high level of compliance to smoke free provisions of the legislation as a result of increased awareness among general public and custodians of public places. Robust enforcement mechanism established. Pro-active district administration involved all important stakeholders led to this historic achievement. The administration has declared Tehri as first smoke free district of the state. This model has motivated and speeds up the Implementation mechanism of tobacco control in entire hilly and difficult state.

PD-658-27 How risky are the innovative strategies that involve community health volunteers in sputum sample collection, packaging and transportation in Mombasa, Kenya?

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Background and challenges to implementation: Kenya notified 89 211 TB cases in 2014 that accounted for only 80% of cases according to estimates by World Health Organization. Mombasa County notified 4726 TB cases with TB case notification rate of 469 per 100 000 population compared to the national average of 208/100 000. With The Global Fund support Amref Health Africa implemented active TB case finding in Mombasa through Christian Health Association of Kenya as the sub-recipients according to Kenya's Strategy for Community Health.

Intervention or response: Community Health Volunteers (CHVs) were trained and mentored on community education, TB screening, referral of presumptive TB cases, sputum collection and transportation, and infection prevention. They instructed and demonstrated to clients how to collect sputum in poly pots and place them in safe containers. CHVs transported samples to the laboratories in cooler carrier boxes. A structured questionnaire to assess risk of CHVs contaminating

themselves with sputum was administered to 37 CHVs, a representative sample of 114 active CHVs, at 14 months of implementation from July 2014 to September 2015. Risk based on frequency of negative practice occurring was classified as: none (never); low (1 in ≥ 10); high (1 in 3–9); very high (1 in 1–2).

Results and lessons learnt: Of the 16 226 sputum samples sent to the laboratory, 870 (5%) were positive for TB. Only 73% of CHVs applied hand sanitizer despite 94% wearing gloves all the time when handling sputum. Laboratory personnel never assisted 45.9% of CHVs in disinfection of their containers and 48.6% of CHVs used only the safety container to transport sputum due to stigma.

Conclusions and key recommendations: With proper training, mentorship and availability of safety commodities CHVs can adopt personal safety practices. However significant risks of contamination still exist and more safety interventions and technical assistance from laboratory personnel are required.

Table Level of risk of contamination of CHVs by source

Source of risk	%CHVs reporting contamination			
	None	Low	High	Very high
Client contaminating poly pot	35.1	51.4	0	13.5
CHV contaminating safety container and carrier during packaging	59.5	29.8	8.1	2.6
Spillage into safety container and carrier during transportation	62.2	22	13	2.8

PD-659-27 Working with empowered community health volunteers and community health workers as a cornerstone to intensify active case finding in Kajiado

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Background: Kenya is ranked 13th among the 22 high burden countries which contribute to 80% of the global TB burden. Over the last ten years, the country has witnessed a tenfold increase in the number of TB cases; this is despite having met the two targets of case detection and treatment success in 2009. Empowering TB and TB-HIV co-infected patients in intensifying improved case-finding has resulted in more identification and notification of suspects at community level. This has resulted in timely diagnosis and thus appropriate treatment.

Methods: Through BMSF funding wave TALAKU in collaboration with DLTD identified 40 community volunteers, 8 community health workers and laboratory locum staff to intensify active case finding in central in Kajiado county Kenya. These teams used approaches like door to door, contact investigation, referral of suspects, community dialogue forums and consented to household visits. Sputum collection from suspects, screening was also done through TB-HIV support groups based on peer

to peer referrals among others. Participants received results with referrals to government clinics and private clinics for TB treatment and Isoniazid preventive therapy as indicated.

Results: During quarter two of the year 2015 the community health workers were able to screen and refer 3207 suspects for TB screening of which 171 had all forms of TB with 3 having smear positive PTB. Through the 4 screening camps organized, 1173 presumed cases were screened, with one being smear positive. Community mobilization through door to door was also enhanced resulting in increased number of suspects.

Conclusions: Among the approaches selected above, intensified case-finding (ICF) in household contacts of TB patients resulted in accelerated detection of both TB and HIV in undiagnosed contacts, thus breaking the cycle of transmission among the two high risk groups. Working with TB and TB-HIV patients proved to be an important component of enhancing case finding. It is also important to note that ICF in household contacts of TB contacts is a feasible approach which identified an extremely high prevalence of previously-undetected TB among smear positive patients. Communities when engaged are critical partners in the fight against TB, resulting in better treatment outcomes.

PD-660-27 Role of rural health care providers in TB prevention and care: experience from a civil society initiative, India

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Background and challenges to implementation: People living in rural areas of India depend mostly on non-formally trained Rural Health Care providers (RHCPs) for health care services including TB. RHCPs are often the first point for health care services in many villages, especially in tribal and remote geographic areas with limited availability of public health services.

Intervention: Project Axshya, under International Union Against Tuberculosis and Lung Disease, is a unique initiative working towards improving access to quality TB care through partnership between government and the civil society especially for women and children, marginalized, vulnerable and TB-HIV co-infected populations. The project has initiated interventions to engage the RHCPs by sensitizing them on TB symptoms and encouraged them to refer such TB symptomatics to the nearest sputum examination facility, the district microscopy centres (DMC), for early diagnosis and treatment.

Results: Project Axshya is bringing RHCPs closer to the national TB control programme by training them to identify and refer TB symptomatics for sputum examination, facilitate sputum collection and transportation and serve as DOT providers. During the period between April 2013 and September 2015, 25 331 RHCPs have been trained. Of this number, nearly 4921 are currently engaged in referring TB symptomatics, sputum collection

and transportation and as DOT providers. They have contributed in identification of 136 535 TB symptomatics and examination of 90 229 (66%) and 10 783 (12%) found to have TB and put on treatment. In the cost analysis of this intervention it was found that the project has invested nearly half a dollar for identification of one TB symptomatic and US \$5 for identifying one TB patient.

Conclusions and key recommendations: The results of this intervention clearly indicate that training and engagement of RHCPs can be done in a cost efficient manner. Also the results showed that RHCPs have become good linkages between national TB control programme and community with early gains in programme outcomes. The project has proved that sensitisation of RHCP and engaging them in TB care and control will help in enhancing the TB Case detection in rural areas and they can be used as an extended hand of public health system.

PD-661-27 Gender differences in disclosure among TB-HIV patients reporting to some health facilities in the Greater Accra region of Ghana

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Background: One of the challenges of tuberculosis (TB) treatment is non-adherence, attributable to non disclosure for fear of being stigmatised. The study sought to explain the gender differences in patterns of disclosure among patients receiving treatment for TB and Human Immunodeficiency Virus (HIV) and how these impact on treatment adherence.

Methods: The study was conducted in Ghana, using six health facilities in the country's capital from July 2013 to February 2014. The study design was descriptive design and a mixed method was adopted; quantitative and qualitative methods using survey and in-depth interviews respectively. A total of 310 respondents (198 males and 112 females) were sampled for the survey. Thirty (30) participants made up of 24 (12 males and 12 females) TB-HIV patients and 6 health workers were purposively selected for the qualitative study. STATA 12 was used in generating frequency distribution tables generated based on gender. For the qualitative study nodes were created by coding test in Nvivo 10 for analysis.

Results: The study found that disclosing TB-HIV status was a challenge especially among women. It was found that more males than females disclosed their status to their partners, 70% and 63.8%, and members of their community 15.3% and 30.8%, respectively, whilst more females than males disclosed their status to family members, 57.1% and 43.4% respectively.

The effect of such disclosures also lead to partners abandoning their sick partners leading to missing medication on the part of the males. The women in the study, except a few, were able to circumvent the

challenges of the treatment regimen and are able to adhere to their treatment regimen.

Conclusions: Disclosing one's TB-HIV status is influenced by gender dynamics in relationship to the circumstances women and men find themselves at one point in time. Strategies need to be developed to avert the problems associated with non-adherence to TB treatment such as multi-drug resistance TB in an effort to control TB in Ghana. It is recommended that TB centres liaise with the Ministry of Gender and Social Protection to put measures like weekly/monthly stipends to support patients who are abandoned by relations.

PD-662-27 Achievements in smoke-free area implementation and ban on tobacco advertising, promotion and sponsorship in Kulon Progo District, Indonesia: an effort to protect public health

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Background and challenges to implementation: Kulon Progo condition before its issued the local regulation of Smoke Free Area (SFA) in April 2014, same with another districts in Yogyakarta, no rules for SFA and TAPS ban. In 2013 the Muhammadiyah District Boards urged the Regent to issue the tobacco control concerning to reduce tobacco use, and protect the children from the cigarettes smoke exposure, and prevent youth and children to start smoking. The challenge was the tobacco control issue is not familiar issue, and people thought that the substance of SFA Regulation will prohibit planting tobacco, selling tobacco leafs, and producing cigarettes are prohibited. The large number of tobacco farmer and the cigarette factories also the obstacle that Regent should be dealing with.

Intervention or response: There are two programme had addressed to Kulon Progo are Support local government of Kulon Progo District in developing academic paper and drafting smoke-free bill; and capacity building Smoke Free Environments and ban TAPS. In April 2014, officially Kulon Progo Government issued the Local Regulation of SFA Number 5 Year 2014. Ban designated smoking room including selling, promotion, and advertisement of cigarette inside building. A Capacity Building on smokefree enforcement, implementation, monitoring, and evaluation with complete ban of tobacco advertising and promotion was conducted inviting the Smoke Free Agents from sub-districts level.

Results and lessons learnt: In December 2015, a compliance study was conducted to evaluate progress of SFA Implementations and TAPS Ban. The compliance rates of a 'no smoking sign' at the main entrance in the work places are low. For example, the compliance rates in work places is from less than 5% increase to 38%. However, the compliance of 'no cigarettes selling activities indoor' is high, 2%. In March 2016, Kulon

Progo was free from tobacco advertising outdoors, replaced with the Public Health Messages.

Conclusions and key recommendations: The Kulon Progo achievement is the good lesson learn to other districts in Indonesia. The degree of compliance rates can be used to stimulate active enforcement. Results may also identify gaps in implementation planning and indicate types of activities that require more targeted intervention.

PD-663-27 Concept of Axshya Village, a tuberculosis-free village: a potential End TB strategy

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Background: The monster that lurks in the shadows is what needs to be tackled! There are one million missing TB cases in India which remain undiagnosed, untreated and continue to infect community. Moving towards the goal of END-TB, it's imperative to reach missing millions through sustainable community-driven mechanisms.. Thus, Project Axshya introduced the concept of Axshya Villages i.e. TB free 'model villages'. The communities here commit to control TB and move towards becoming TB-free. Every villager is aware of TB, facilities, diagnosis and management. They support each other to seek timely care and complete treatment under RNTCP and all efforts are made for a successful outcome.

Intervention: Project Axshya, coordinated by The Union, is a civil society initiative to strengthen TB care and control in India. Axshya villages are those wherein the project team identifies vulnerable and marginalised rural community, undertakes several interventions (outlined in Table) to sensitize all the residents about TB and TB services engaging them in TB control efforts and subsequently declares it as a model village.

Results: 8661 model Axshya villages have been established during the period April 2013–September 2015. Each household in such villages has been reached out through various activities including Axshya SAMVAD, community meetings and mid-media activities.

Conclusions: 100% of the population in Axshya villages is sensitised about TB and related services empowering them to take active role in TB control efforts. This enhances the role of community towards END-TB efforts and is a potentially powerful strategy towards that end.

Table Activities in Axshya Village

Axshya Mitras Are motivated volunteers from the village who are interested in providing services of TB in community. They carry out activities like: Community meetings, Mid media activities, Axshya SAMVAD or Intensified Outreach Activity, Linking with RNTCP services - Referral/Sputum Collection and transportation and delivery of results to patients, Follow-up with RHCPs, DOT provision and Treatment adherence. Thus they mobilize community for TB care and control.

Axshya SAMVAD Axshya Mitras visit households, inform them about TB, its symptoms, diagnosis, and treatment and RNTCP services, link the identified TB symptomatic and diagnosed TB patients to RNTCP services through referral and/or, Collection and transportation of sputum samples to the DMC for diagnosis and/or treatment. Axshya Mitras will cover 25 households per day.

Mid Media Disseminating TB related messages to communities at large by street plays, wall paintings, local cable television network, sensitization in school college, miking and rally on TB, taxi, train bus etc. displays and health camps.

Community Meetings Are Gaon Kalyan Samitis (GKS), PRI Members (PRI), Mahila Mandals (MM), Community Based Organisation (CBO), Self Help Groups (SHGs), schools and other similar groups. They meet regularly in the village level to address myths and misconceptions and help symptomatic persons seek timely appropriate care.

07. Issues surrounding TB: 'Medicines make you feel good though they can also make you feel sick'

PD-664-27 Systematic review and meta-analysis of the effect of fluoroquinolones on time to culture negativity in drug-susceptible tuberculosis

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Background: Improved sterilization of TB drug regimen is important both for individual patients and TB programmes. We conducted a systematic review and meta-analysis of the effect of fluoroquinolones on time to culture and smear-negativity and molecular outcomes. **Methods:** A compound search strategy to identify all relevant clinical trials was performed limited to studies published between January 2000 and October 2015. MEDLINE, EMBASE, Global Health, Cochrane, Web of Knowledge and Clinical trials were searched. Proportion of culture, smear and molecular conversion were extracted and a pooled meta-analysis was performed on similar time points since initiating treatment.

Results: 78/2399 identified abstracts were included for full text review. Of those 14 were included in the qualitative systematic review and 12 contributed to the quantitative meta-analysis. The proportion culture negative in moxifloxacin containing regimens at 4, 6, 8 and 12 weeks was 45% (95%CI 42–49, 4 studies), 79% (95%CI 76–82, 3 studies), 91% (95%CI 90–93, 10 studies) and 99% (95%CI 95–100, 1 study). Risk ratios (RR) comparing proportion of culture conversion in

moxifloxacin-containing regimens with standard regimens for 4, 6, 8 and 12 weeks were 1.6 (95%CI 1.3–1.9, 4 studies, I² = 33%), 1.3 (95%CI 1.2–1.5, 3 studies, I² = 0%), 1.1 (95%CI 1.0–1.1, 10 studies, I² = 28%) and 1.02 (95%CI 0.99–1.09, 1 study). For gatifloxacin-containing regimens the proportion culture converted at 4, 8 and 12 weeks was 21 % (95%CI 15–27), 85% (95%CI 83–87) and 96% (95%CI 91–98), respectively (Figure 1). Two studies using moxifloxacin and gatifloxacin-containing regimen showed similar smear conversion at 8 weeks compared to standard regimen (RR = 1; 95%CI 0.8–1.3 and RR = 0.99; 95%CI 0.95–1.03). No study reported on molecular outcomes.

Conclusions: The earlier sterilizing effect seen with regimens containing moxifloxacin is important in the context of onwards transmission during therapy. To assess this effect in all fluoroquinolone containing regimens and in the context of newer molecular diagnostics an individual patient-level data meta-analysis is needed.

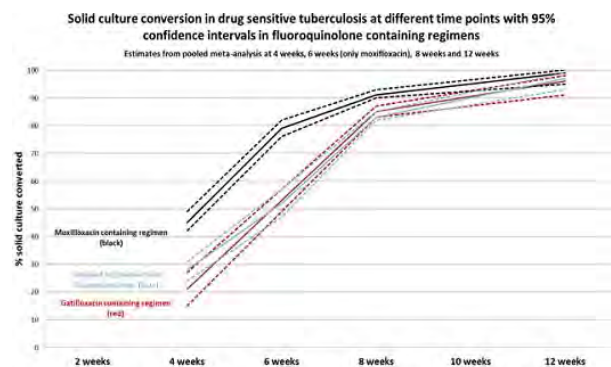


Figure 1a Culture conversion at week 4, 6, 8 and 12 with 95% Confidence intervals in a meta-analysis of RCTs with moxifloxacin and gatifloxacin containing regimens (outer and inner line: 95% Confidence intervals)

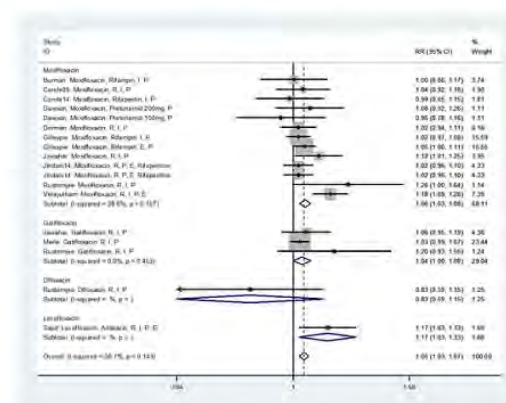


Figure 1b Meta-analysis of patients culture converted at week 8 with fluoroquinolone-containing regimens compared to standard therapy in drug sensitive tuberculosis

PD-665-27 The effectiveness of inhaled nebulized chemotherapy in patients with newly diagnosed pulmonary tuberculosis with concomitant tuberculosis of trachea and bronchi

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Background: The aim of the research was to determine the effectiveness of TB treatment with the addition of isoniazid and rifampicin inhalations via nebulizer in patients with pulmonary TB with concomitant TB of trachea and bronchi.

Methods: 48 patients with respiratory TB were divided into two groups: the main group (MG), $n = 21$ and the control group (CG), $n = 27$. Patients in MG received standard chemotherapy and further 0.15 g of isoniazid and rifampicin 0.15 g inhaled through a nebulizer, also they received salmeterol 50 mcg + fluticasone propionate 250 mcg at 2 breaths twice a day for 2 months. Patients in CG received standard TB treatment.

Results: After 1 month sputum conversion was found in 14 (66.7%) patients in MG and 10 (37.0%) patients in CG, $P < 0.05$. On completion of the intensive phase (IP) sputum conversion was observed in 19 (90.5%) patients MG and 21 (77.8%) in CG, $P > 0.05$. The average time of sputum conversion was 1.4 ± 0.3 months in MG, and 2.5 ± 0.4 months in CG, $P < 0.05$. Cavity healing occurred after 2 months of treatment in 13 (61.9%) patients in MG and 12 (44.4%) in CG, $P > 0.05$. Large residual changes in the lungs: 5 (23.8%) patients MG and 18 (51.9%) CG, $P < 0.05$. After completion of treatment scar stenosis of the bronchi II-III art. diagnosed in 3 (14.3%) patients MG and 17 (63.0%) in CG, $P < 0.05$. The duration of hospital treatment was 2.4 ± 0.4 months in MG and 3.9 ± 0.5 months in CG, $P < 0.05$.

Conclusions: The use of inhalation drugs IP of chemotherapy in patients with pulmonary TB increases the frequency of sputum conversion on 29.7% for the 1st month of treatment, reduces the incidence of scar stenosis of the bronchi II-III art. on 38.7%.

PD-666-27 Usefulness of moxifloxacin in tuberculous meningitis

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Background: Due to poor penetration of anti-tuberculosis drugs to the central nervous system it is necessary to consider alternative pharmacological looking for faster disease control. Objective of this study is to establish the safety of moxifloxacin as part of treatment in tuberculous meningitis.

Methods: A cohort study was conducted among two groups of patients with tuberculous meningitis, one of

them ($n = 24$) received conventional scheme while the other one ($n = 23$) received moxifloxacin instead of ethambutol. Glycorrhagia and Mycobacterium tuberculosis polymerase chain reaction (PCR) in cerebrospinal fluid were requested during the first and second month of treatment.

Results: While all patients receiving moxifloxacin showed negativity in PCR of cerebrospinal fluid samples obtained after the first month of treatment, it remained positive in 50% of the cohort that received ethambutol; glycorrhachia was normalized in 90% of group receiving moxifloxacin and in 20% of patients in the other group; during the second month PCR remained positive in 6 cases and persistent hypoglycorrhachia in 5 cases the group receiving ethambutol. Resistance to first-line drugs was not documented.

Conclusions: Given the better penetration of moxifloxacin to the central nervous system, this should be considered as an alternative to ethambutol due to the low penetration of the latter into inflamed meninges.

The fastest improvement in CSF glucose and molecular tests negativization observed in patients receiving moxifloxacin justify their prescription as first-line drug in tuberculous meningitis.

PD-667-27 The use of moxifloxacin in the treatment of patients with pulmonary TB associated with viral hepatitis B and C

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Background: The purpose of this research was to study the efficacy and tolerability of chemotherapy regimen with the use of moxifloxacin instead of pyrazinamide in patients with pulmonary TB and concomitant viral hepatitis B and C.

Methods: A controlled, randomized study included 60 patients with newly diagnosed pulmonary TB smear+ with concomitant viral hepatitis B and C. Patients were randomized into 2 groups (30 patients in each). Patients of the main group (MG) received chemotherapy regimen, in which moxifloxacin 7.5 mg/kg was administered instead of pyrazinamide because of its intolerance in the intensive phase. In the control group (CG) the standard chemotherapy regimen was prescribed: isoniazid, rifampicin, ethambutol, pyrazinamide in standard doses. Patients in both groups were comparable in terms of forms of disease, prevalent form was infiltrative pulmonary TB; 56.4 and 54.9%, respectively, the remaining patients had disseminated pulmonary TB ($P > 0.05$). With the same frequency determined destruction of the lungs (47.2 and 50.0% in MG and control, respectively).

Results: The effectiveness of moxifloxacin instead of pyrazinamide in the intensive phase of treatment was significantly higher in terms of sputum conversion (72.6% in MG vs. 47.2% in the CG, $P < 0.05$), the regression of clinical symptoms and resorption infiltrative changes in the lungs (81.2% in MG vs 52.6% in the CG, $P < 0.05$). The frequency of side effects to anti-tuberculosis drugs was significantly lower in MG (34.3% in MG vs. 56.2% in CG, $P < 0.05$). In MG severe side effects, requiring the cancellation of ongoing TB treatment, were significantly less (3.2% vs. 26.7% CG, $P < 0.05$).

Conclusions: Inclusion of moxifloxacin instead of pyrazinamide in the scheme of TB treatment of in patients with accompanying viral hepatitis B and C made it possible to increase the frequency of sputum conversion till the time of completion of the intensive phase of chemotherapy, and to reduce incidence of side effects (from 46.4% to 34.6%), as well as the severity of their symptoms, thus ensuring continuity of chemotherapy

PD-668-27 The impact of hepatitis C co-infection on tuberculosis drug-induced liver injury

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Background: In 2013–2014, there were 140/3860 (3.6%) patients at the Singapore TB Control Unit who had TB treatment interrupted due to presumed drug-induced liver injury (DILI), defined as ALT/AST elevation $> 2X$ upper limit normal (with/without symptoms). Hepatitis Bs antigen and anti-hepatitis C serology were performed for these patients. Of these, 20/140 (14.3%) were hepatitis C positive (HepC+), 16/140 (11.4%) were hepatitis B positive, 8/140 (5.7%) had alcoholic liver disease. We determined the impact of hepatitis C co-infection on the treatment course and outcome of a cohort of patients with TB-DILI.

Methods: TB patients at the TB Control Unit with treatment interruption over 2013–2014 because of DILI were identified through the Singapore National TB Registry. Case records were perused for demographics, investigations and treatment regimens. The course of DILI was compared between HepC+ patients ($n = 20$) and patients without chronic liver disease ($n = 92$).

Results: The median time to treatment interruption/DILI was 5.1 (range 0–31.9) weeks vs. 9.9 (range 1.7–33.9) weeks for DILI patients without chronic liver disease and with HepC+ respectively ($P < 0.001$). The median maximum ALT /AST was 176/190 u/l vs. 215/183 u/l; median time to recovery/normalization of ALT/AST was 3.0 weeks vs. 6.3 weeks ($P < 0.001$); and median duration between treatment interruption and treatment restart was 1.7 weeks vs. 3.0 weeks ($P < 0.001$) in those DILI without chronic liver disease and with HepC+ respectively. More HepC+ DILI patients had their

treatment interrupted after ≥ 8 weeks compared to without chronic liver disease: 14/20 (70.0%) vs. 27/92 (29.3%) respectively ($P = 0.001$). DILI patients without chronic liver disease {84/92 (91.3%)} vs. {16/20 (80%)} with Hep C+ have completed their treatment ($P = 0.14$). There was no difference in the adjusted treatment regimens after DILI recovery: 63.7% without chronic liver disease vs. 65.0% with HepC+ had 1 or 2 hepatotoxic drugs removed in the re-introduction regimen.

Conclusions: TB treatment interruption due to DILI in patients with hepatitis C co-infection occurred later. Most had completed 2 months of pyrazinamide-containing intensive phase before DILI onset. They had slower recovery of transaminitis but could tolerate similar re-introduction regimens compared with DILI patients without chronic liver disease.

PD-669-27 Non-linear increase in exposure following higher rifampicin doses characterized by saturation in the elimination as determined using population pharmacokinetic analysis

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Background: Accumulating evidence suggests that increasing the dose of rifampicin may reduce treatment times for pulmonary tuberculosis. In a recent multiple dose rising trial (Boeree, et. Al., Am J Respir Crit Care Med, 2015), rifampicin was well tolerated at 40 mg/kg daily, however, unexpectedly high exposures were observed at the higher doses. Our objective was to characterize the non-linear exposure using non-linear mixed effects modeling in order to assist in optimizing the rifampicin dose.

Methods: Data consisted of plasma pharmacokinetic samples from 83 pulmonary tuberculosis patients given daily rifampicin of 10 (reference arm, $n = 8$), 20, 25, 30, 35 or 40 ($n = 15$ /arm) mg/kg for 14 days, as monotherapy for 7 days and combined with isoniazid, pyrazinamide and ethambutol for the following 7 days. Blood samples were drawn at days 7 and 14 with rich sampling between 0 and 24 hours. Data were analysed in NONMEM 7.3. Models were chosen using the likelihood ratio test and diagnostic plots. Rifampicin auto-induction was accounted for by a previously developed enzyme turn-over

model and a recent estimated enzyme turn-over half-life. Non-linearity in exposure was evaluated in clearance and bioavailability. Concentration-dependency was evaluated in clearance using linear and Michaelis-Menten relationships. Dose-dependency was evaluated in bioavailability using linear and Emax relationships. Different absorption models were evaluated.

Results: A one-compartment model, a transit absorption compartment model and a Michaelis-Menten relationship on clearance described exposure in all dose groups and at the two occasions (days 7 and 14). Model predicted fold increase in AUC_{0-24h} compared to a standard 10 mg dose in a typical patient (54 kg) at day 14 was 2.6, 4.0, 5.6, and 8.0 for 20, 30, 40 and 50 mg/kg of rifampicin, respectively.

Conclusion: The developed rifampicin population pharmacokinetic model accounted well for exposure-dependent auto-induction and non-linear decrease in clearance at higher doses. This finding should be taken into consideration when designing future trials. The model allows for clinical trial simulations of even higher doses in order to optimize the rifampicin dose.

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PD-670-27 Variability in adverse event grading scales used to assess the safety of high-dose rifampin in TB trials

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Background: The reported frequency of hepatotoxicity among patients receiving rifampin for treatment of tuberculosis has been highly variable. Whether variability is related to dose, dosing frequency, or is idiosyncratic remains the subject of debate. Studies investigating high-dose rifampin to shorten tuberculosis treatment duration aim to resolve uncertainty around the relationship between rifampin doses and hepatotoxicity. These trials, however, relied on three different scales for grading adverse events (AEs). RIFATOX used the Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric AEs; HIGHRIFF1, HIGHRIFF2, and MAMS-TB-01 used the National Cancer Institute's Common Terminology Criteria for AEs (CTCAE); and HIRIF used the Division of Microbiology and Infectious Diseases (DMID) Adult Toxicity Table. Here, we highlight expected differences in frequency and distribution of AE grades due to divergent grading cutoffs.

Methods: We compare grading thresholds for liver enzymes (aspartate aminotransferase [AST], alanine aminotransferase [ALT], alkaline phosphatase [ALP],

and bilirubin) across the three scales. Frequency of Grade 3 and 4 events will be compared across HIGHRIFF2 and HIRIF, and then standardized to both CTCAE and DMID scales.

Results: Thresholds vary for nearly all grades and enzymes. Asymptomatic AST/ALT values 3 times the upper limit of normal (ULN) equate to Grade 1, Grade 2, and Grade 3 across scales. Elevated AST/ALT/ALP are Grade 4 if >8.0 times ULN for DMID, 10.0 times ULN for DAIDS, and >20.0 times ULN for CTCAE (see Table). With 180 participants each, HIGHRIFF2 observed one Grade 3 elevated enzyme while HIRIF observed 22 Grade 3 and four Grade 4 elevated enzymes.

Conclusions: Caution should be exercised in interpreting results on frequency and distribution of liver toxicity across tuberculosis trials—choice of scale may increase the number of events reported. Trialists could use a single grading scale and include the scale in the supplement of manuscript.

Table Comparison of liver enzymes across grading scales –

Hepatic enzymes	AE grade	CTCAE	DAIDS	DMID
AST, ALT	1	>1.0–3.0 x ULN	1.25–<2.5 x ULN	1.1–<2.0 x ULN
	2	>3.0–5.0 x ULN*	2.5–5.0 x ULN	2.0–<3.0 x ULN
	3	>5.0–20.0 x ULN*	5.0–<10.0 x ULN	3.0–8.0 x ULN
	4	>20 x ULN	≥10.0 x ULN	>8.0 x ULN
ALP	1	>1.0–2.5 x ULN	1.25–<2.5 x ULN	1.1–<2.0 x ULN
	2	>2.5–5.0 x ULN	2.5–<5.0 x ULN	2.0–<3.0 x ULN
	3	>5.0–20.0 x ULN	5.0–<10.0 x ULN	3.0–8.0 x ULN
	4	>20 x ULN	≥10.0 x ULN	>8.0 x ULN
Bilirubin	1	>1.0–2.5 x ULN	1.1–<1.6 x ULN	1.1–<1.5 x ULN*
	2	>2.5–5.0 x ULN	1.6–<2.6 x ULN	1.5–<2.0 x ULN*
	3	>5.0–20.0 x ULN	2.6–<5.0 x ULN	2.0–3.0 x ULN*
	4	>20 x ULN	≥5.0 x ULN	>3.0 x ULN*

* All values presented are for asymptomatic events; scales offer alternate grading thresholds when these values are accompanied by specific symptoms.

PD-671-27 Adverse reactions associated with second-line anti-tuberculosis drugs among patients with M/XDR-TB in Tbilisi, Georgia

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Background: Second-line anti-TB drugs used to treat M/XDR-TB often cause adverse drug reactions (ADRs). Given that the frequency of ADRs among patients in Georgia and the impact on clinical care has not been previously assessed we sought to determine the rates of and risk factors for ADRs among M/XDR-TB patients.

Methods: A cohort of patients who initiated treatment for M/XDR-TB at the National Center for Tuberculosis and Lung Diseases, Tbilisi, Georgia, between July 2010 and December 2012 were included. Data were abstracted from medical and laboratory records using a standardized form. Multivariate analysis was performed to assess predictors of ADRs.

Results: Among 147 patients with M/XDR-TB, the median age was 35 years (range 17–73), and 65% were male. HIV co-infection was found in 5%, 12% had diabetes and 20% had a positive anti-hepatitis C antibody. Nearly all patients (99%) had ≥ 1 ADR; the median was 9 (range 0–24). The most common ADRs included nausea (91%), vomiting (79%), abdominal pain (74%), and arthralgias (65%). Serious ADRs, such as psychosis (31%), nephrotoxicity (26%), ototoxicity (26%) and drug-induced hepatitis (15%), were also common. A change in drug dosing due to an ADR occurred among 14 (10%) patients, while 54 (37%) patients required temporary and 92 (63%) patients required permanent interruption of ≥ 1 drug. Drug interruption due to ADRs occurred most frequently with prothionamide (44%) followed by pyrazinamide (21%), kanamycin or capreomycin (16%), and PAS (13%). Older age ($P < 0.001$) and being female ($P = 0.04$) were associated with an increased number of ADRs. The presence of bilateral pulmonary tuberculosis ($P = 0.03$), impaired hearing ($P = 0.01$), gastritis ($P = 0.04$), vomiting ($P < 0.001$) and vertigo ($P = 0.03$) were associated with increased number of permanent drug interruptions per patient.

Conclusions: ADRs were very common among patients undergoing treatment for M/XDR-TB. An increased number of ADRs was seen among older patients and women with M/XDR-TB. The high rates of ADRs frequently led to drug interruptions. Independent risk factors for increased number of permanent drug withdrawals included the presence of bilateral pulmonary tuberculosis, impaired hearing, gastritis, vomiting and vertigo.

PD-672-27 Local therapy for non-specific endobronchitis in patients with pulmonary tuberculosis

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Background: The epidemiological situation for tuberculosis (TB) in Russia remains stressful. In Yakutia, there is an increasing trend in culture-positive pulmonary TB cases with destructions in lung tissue. Destructions in lung tissue often involves the bronchi, this condition is labelled as nonspecific endobronchitis (NE). For NE to be treated more effectively, local therapy, such as intratracheal medication administration, seems preferable. We propose a method for intratracheal administra-

tion of synthetic immunomodulatory agent Bestim, which is quickly absorbed into the lymph, then into pulmonary circuit, and is retained in the interstitial tissue. The method is patented (Russian Federation Patent 2450820, publication date May 20, 2012).

Methods: Patients with destructive pulmonary TB with concurrent NE received Bestim (1 mg diluted in 2 ml of 0.9% NaCl solution; intratracheally; thrice a week, on alternate days, during 2 weeks; 6 injections per 1 course), on top of standard chemotherapy prescribed based on drug-sensitivity (DS) profile of *M. tuberculosis*. The experimental group included 27 patients, who received chemotherapy based on DS profiles plus intratracheal Bestim. The control group included 20 patients, who received standard chemotherapy based on DS profiles without Bestim. Treatment effectiveness was assessed in terms of bacterial isolation cease, healed destructions, immunological parameters (T-cells, IL4, IFN-gamma, TNF-alpha), and results of bronchoscopy. Results were statistically significant at $P \leq 0.05$.

Results: By the end of the intensive phase, bacterial isolation cease was established in 25 (92.6%) patients in experimental group vs. 10 (50%) in control group. Healed destructions were observed in half of the patients in experimental group vs. 5 (25%) in control group. In group 1, NE was cured in all patients by the end of the first month of therapy, vs. 2 months in the control group. In group 1, after 2 months of therapy, we noted reliable increase in CD4+ ($P < 0.05$; mean level $33.2 \pm 3.7\%$), trend to normalization of the levels of IL4 and IFN-gamma, and reliably decreased levels of TNF-alpha ($P < 0.05$).

Conclusions: Use of Bestim on top of standard anti-TB chemotherapy allowed improvement of treatment effectiveness, in particular, achievement of bacterial isolation cease and healed destructions in shorter time (2 months).

08. Knowing the enemy: MDR-TB epidemiology I

PD-673-27 Evaluation of drug-resistant tuberculosis surveillance, Botswana, 2014

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Background: In 2008, 2.5% of new tuberculosis (TB) cases in Botswana were multidrug-resistant (MDR). The Botswana National TB Program uses paper registries and 2 electronic TB surveillance systems—Electronic TB Registry (ETR.Net) for drug-susceptible TB and OpenMRS for drug-resistant TB— but plans to consolidate all TB surveillance into OpenMRS to reduce costs. We evaluated Botswana's drug-resistant TB surveillance system in order to suggest program improvements and inform future electronic consolidation.

Methods: We abstracted data from paper registers for 2011 and 2013 at 3 of 5 drug-resistant TB treatment facilities. We compared data from paper registers and OpenMRS to determine completeness of patient entry and selected TB indicators. We interviewed key stakeholders (program staff, TB controllers, and MDR-TB clinicians) about surveillance system acceptance, simplicity, usefulness, flexibility, and timeliness.

Results: Data for 113 registered patients (100%) were abstracted from paper registers. Percentages for completeness of demographic variables were 95% (107/113) for birthdate, 98% (111/113) for gender, and 97% (110/113) for HIV status. Percentages for completeness of laboratory data were 20% (23/113) for smear, 23% (26/113) for culture, and 53% (60/113) for drug-susceptibility test results. OpenMRS contained data on only 47% (52/113) of patients, and percentages of completeness varied from 52% (27/52) for HIV status to 100% (52/52) for birthdate. Interviews with stakeholders elucidated differing opinions on whether to use OpenMRS as a surveillance database or as both a surveillance database and an electronic medical record.

Conclusions: Variability in complete reporting of drug-resistant TB indicates the need to give priority, before consolidation, to improving the completeness of reporting in OpenMRS. Additionally, the role of OpenMRS needs to be clearly defined, and agreement is needed from all stakeholders.

PD-674-27 Understanding the profile of multidrug-resistant TB patients in Delhi, India

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Background: Population Services International (PSI) in collaboration with RNTCP piloted psychosocial counselling intervention across 28 districts in India as part of Project Axshya. One of the major challenges in the management of MDR-TB is preventing patient loss to follow-up (LTFU). Understanding the profile of MDR-TB patients would help to assess the needs of MDR-TB patients for better planning of psychosocial counselling to prevent loss to follow up and ensure treatment adherence.

Methods: We conducted a retrospective analysis of counselling case files of MDR-TB patients registered in Motinagar district tuberculosis centre at Delhi. Total 121 MDR-TB patients registered case files between May 2014 to October 2015 were analysed. Analysis was done through descriptive statistics using MS-Excel.

Results: Of the total ($n = 121$) MDR-TB patients registered, 63% were between the age group of 15–29 yrs. Out of which 55% male and 45% were female patients. The average monthly income of MDR-TB patients was less than US \$110 per month and around 59% were financially dependent on other family members. Of the total ($n = 121$) 60% of the patients were tested for TB two years before registering at the

centre, where 44% were tested in private and 56% were tested in Government health centres. More than half of them had not been exposed to TB through contacts outside their households. 97% of the patients counselled were tested for HIV, however only 34% were tested for Diabetes. Of total tested for diabetes ($n = 41$) 6% of were detected diabetic.

Conclusions: The analysis provided information on profile of MDR-TB patients registered at the centre, more than half of patients were not working and dependent on others for financial help, the average monthly income was less than sufficient to support the personal needs, let alone the nutrition supplements. This indicated the need for linkages to social welfare schemes, nutrition support and even livelihood support. Looking at low percentage of diabetes testing, there is need for diabetes testing among MDR-TB patients to rule out co morbidities.

PD-675-27 High prevalence of drug-resistant tuberculosis reported from a hilly, remote district of India under the Revised National TB Control Programme

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Background: TB is a major public health problem in India. Of the estimated 9.6 million new TB cases in 2014 globally, India accounts for almost one-fourth (23%). Moreover, an estimated 64 000 multidrug-resistant TB (MDR-TB) cases occur annually in India among notified pulmonary TB cases. Previous drug resistance studies in India suggest that MDR-TB prevalence is 2–3% among new cases and 12–17% among reinfection cases. Sikkim-East is a small hilly remote district in state of Sikkim, India; with complete Revised National TB Control Program (RNTCP) implementation since March 2002. Sikkim had always maintained the global and national treatment success outcome targets since the inception of the programme. However with the launch of Programmatic Management of Drug Resistance TB (PMDT) increasingly high levels of DR TB is being reported from East Sikkim.

Methods: All the new and re-treatment pulmonary TB cases enrolled under the Revised National TB Control Program from 2012–2015 were tested for the presence of drug resistance TB strains as per criteria laid down by the program.

Results: Of the 1607 pulmonary TB cases enrolled in 2012–2015 under RNTCP, 537 (33%) cases of drug resistance were detected of which 510 were MDR-TB (31%) and 27 (2%) were XDR-TB cases.

Conclusions: Almost one third of the pulmonary TB cases registered under RNTCP during 2012–2015 developed DR-TB. It is higher than the trends reported from other parts of the country raising the question of higher vulnerability of the population to drug resistance. Further studies on the genetic makeup, ethnicity and socio-economic factors of the population under study, despite high treatment initiation with promptness needs to be undertaken to explain these trends.

Year	2012	2013	2014	2105	Total
Total pulmonary TB cases	433	394	395	285	1607
Total MDR cases	119	131	134	126	510 (31%)
Total XDR cases	0	5	4	18	27 (2%)

PD-676-27 Paradigm shift in presumptive DR-TB: MDR-TB diagnosis in Bangladesh

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Background: Bangladesh ranks 13th among the 27 high MDR-TB burden countries of the world in terms of absolute numbers, and 26th in terms of rate. It contributes 1.6% of the global-TB burden. According to the 1st nationwide Drug Resistance Survey (DRS) conducted in 2010–2011, MDR-TB rate among new TB cases is 1.4% (95% CI 0.7–2.5) and 28.5% (95% CI 24–34) among retreatment cases. The total estimated number of MDR-TB in 2015 is 4800 cases. The National Tuberculosis Control Programme (NTP) in Bangladesh started implementing the Programmatic Management of Drug-resistant TB (PMDT) in 2008 using a Green Light Committee (GLC)-approved standard 20-month MDR-TB regimen. PMDT in Bangladesh has expanded countrywide increasing diagnostic and treatment access to patients.

Methods: Data was collected from the routine reporting system of NTP. All MDR/RR-TB patients enrolled in the year 2015 under GLC-approved standard MDR-TB regimen were taken into consideration and descriptive analysis was done to find out the proportion of MDR/RR-TB cases from different categories.

Results: In 2015, A total of 37 741 presumptive DR-TB cases were tested, among whom 14 582 (38%) cases were detected with MTB and 994 were found resistant to Rifampicin. Out of them 880 (89%) were enrolled for MDR treatment. The female/male ratio (0.54:1) among MDR-TB was found to be lower than that observed through routine diagnosis (0.65:1). Data analysis of presumptive MDR-TB sources showed that the highest number of MDR-TB detected (32%) from the cases relapses after category-1 (2EHRZ/4HR) treatment and lowest from lost to follow-up of category-2 regimen (2SEHRZ/1EHRZ/5EHR) (0.6%). Among others non converters of category-1, failures of category-1 and relapse Category- 2 are respectively 25%, 13% and 8%. Only 2% cases are from contact examination of

MDR-TB and 2.6% cases were among extra-pulmonary TB.

Conclusions: Introducing GeneXpert testing among all form of retreatment cases at start of treatment has improved prompt detection of rifampicin resistant thus reduced rifampicin resistant among failures and relapse of category 2 treatment regimens. A low percentage (2%) of cases with contact of DR-TB patients might be a wake up call for to improve contact tracing.

PD-677-27 Trend of fluoroquinolone resistance in MDR cases in Pakistan

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Background: Currently in Pakistan there are 27 MDR treatment sites and more than 2500 patient were enrolled on treatment in 2015. Before 2009 there was only one DST laboratory in private sector currently there are five QA DST laboratories. On detection of Rifampicin resistance using GeneXpert MTB/RIF, patients are put on second line treatment without waiting for DST results. Standard treatment includes levofloxacin which is replaced later by moxifloxacin in case resistance is reported to ofloxacin (2.0 µg/ml). Data on drug resistance is collected from all laboratories on quarterly basis. We present FQ drug resistance trends in MDR strain over last three years

Methods: All DST by public sector laboratories were reported on LJ media till mid 2015 and later on MGIT. One laboratory in the private sector reported DST on MGIT other on agar media. Four laboratories were linked to PMDT treatment sites in different provinces for provision of DST services. All laboratories participate in annual EQA scheme for DST and used recommended critical concentration for each drug based on culture media used

Results: A high FQ resistance is reported in MDR patient both in new and those with history of TB treatment. However in 2015 a decline in FQ resistance from baseline of 45.8% to 36.8% is reported and in previously treated cases, 45.1% was reported in 2015 against 48.0% in 2013. A slight decline in FQ resistance in combination with second line injectable (XDR) is also reported, from 4.5% to 3.9%.

Conclusions: The TB programme needs to closely monitor FQ resistance along with sputum conversion and treatment outcome of patientw enrolled in the PMDT.

Figure Trend 2013 to 2015

	New			Previously Treated			All		
	2013	2014	2015	2013	2014	2015	2013	2014	2015
#MDR strain tested	48	238	446	204	1217	1244	2213	2380	1899
Any FQ resistance %	45.8%	39.1%	36.8%	48.0%	51.2%	45.1%	50.7%	51.1%	43.0%
Any ZLI resistance %	8.3%	5.0%	2.5%	4.9%	7.0%	7.6%	6.3%	8.1%	6.4%
XDR%	8.3%	1.7%	2.9%	4.4%	4.8%	4.3%	4.5%	5.4%	3.9%

PD-678-27 Second-line drug-resistant patterns of *Mycobacterium tuberculosis* in retreatment patients in Khartoum State

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Background: Prescription of second line anti-tuberculosis drugs for multi-drug resistant tuberculosis (MDR-TB) patients was started in 2008 in Sudan. The program was run based on presumed and managed cases empirically. In 2010, Sudan signed the Green Light Committee (GLC) Initiative document to combat MDR-TB by improving access to affordable second-line anti-tuberculosis drugs. This study aimed to determine resistance patterns to second line anti-tuberculosis drugs (SLDs), and to determine the frequency of extensively drug resistant (XDR) *Mycobacterium tuberculosis* isolates.

Methods: A total of 239 sputum specimens were collected from smear positive TB retreatment patients during the period from July 2009 to July 2010. Specimens were pre-treated according to Petroff method. The recovered isolates were tested for sensitivity to first line anti-TB drugs by the 1% proportion method on LJ medium; MDR strains were tested for second line anti-TB drugs sensitivity by 1% proportion method on LJ medium and by Hain GenoType MTB-DRsl Assay. Hain GenoType MTB-DRsl Assay is nucleic acid amplification (NAA) assay based on reverse hybridization with specific oligonucleotide probes on nitrocellulose strips. The Hain GenoType MTB-DRsl assay identifies *M. tuberculosis* complex and detects resistance to fluoroquinolone, second line injectable drugs and ethambutol evident as mutations of *gyrA*, *rrs* and *embB* genes, respectively.

Results: One hundred and forty three mycobacterial isolates were successfully recovered from a total of 239 samples (143/239; 59.8%). Two strains (2/143; 1.4%) were identified as RIF/INH-resistant MOTT, the majority (141/143; 98.6%) were *M. tuberculosis* complex strains. Fifty four strains (54/141; 38.3%) were MDR isolates. Four (4/54; 7.4%) isolates died during subsequent subculture. Five of the MDR isolates (5/50; 10%) showed resistance to at least one second line drug and one isolate (1/50; 2%) was XDR. The XDR strain was concordantly detected by the two methods.

Conclusions: Resistance to second line anti-TB drugs among MDR-TB patients; in Sudan is at 10% levels, while XDR-TB is prevalent at low levels (2%); Nevertheless this can fuel the TB epidemics.

PD-679-27 Drug resistance pattern of patients with multidrug-resistant tuberculosis in South Korea: a multicenter study, 2010-2014

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Background: While increasing the use of genotypic drug susceptibility test, the drug resistance pattern of certain countries or societies became more important in determining the empirical treatment regimens for multidrug-resistant (MDR) tuberculosis (TB) patients. This study was conducted to evaluate the drug resistance pattern of MDR-TB patients in South Korea.

Methods: We retrospectively analyzed the phenotypic drug susceptibility test results of culture confirmed-TB patients from Jan 2010 to Dec 2014 in 7 tertiary referral hospitals in Korea.

Results: In total, 5599 culture confirmed-TB patients (58.3% men, mean age 53.2 ± 21.2 years) were included. 4927 patients (88.0%) were new cases. Of total patients, MDR-TB accounted for 4.4% (216 patients) and 24.1% (162 patients) in new cases and previously treated cases, respectively ($P < 0.05$). In MDR-TB patients, resistance rates of ethambutol and pyrazinamide was 63.8% and 35.7%, respectively. Among fluoroquinolones, resistance rates was similar between ofloxacin, levofloxacin and moxifloxacin (25.4%, 23.3% and 20.5%, respectively). Streptomycin showed highest resistance rate among injec drugs (32.3% vs. 18.0% (kanamycin) and 14.7% (amikacin)). Resistance rates of group 4 drugs were as follows: PAS (31.5%), prothionamide (17.5%) and cycloserine (7.1%). Resistance rate of pyrazinamide, fluoroquinolones, prothionamide and cycloserine was higher in previously treated cases than new cases ($P < 0.05$). Extensive drug resistant (XDR) and pre-XDR-TB accounted for 33.0% of all MDR-TB.

Conclusion: When determining the empirical treatment regimens for genotypically confirmed-MDR-TB patients, high drug resistance rates and resistance patterns should be considered.

PD-680-27 Distribution of MDR-TB cases by residence in Uganda: a time series analysis

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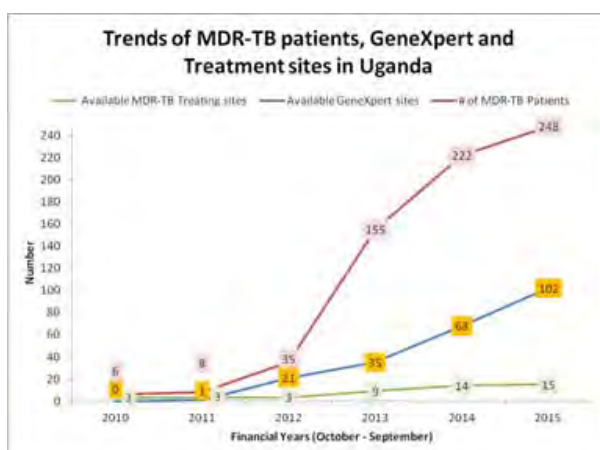
Background: Emerging drug resistant TB (DR-TB) is complicating TB control in Uganda. Estimated prevalence at 1.4% and 12% among new and retreatment cases respectively. We established the spatial distribution and trends of notified DR-TB patients in relation to the available GeneXpert and treatment services in the country over time.

Intervention: We conducted time series analysis of the secondary data of the districts of residence reported by DR-TB patients notified between 2010 and 2015 using Microsoft Excel and plotted it on geographic information system (GIS) Maps to generate their spatial distribution over the years. The available numbers of GeneXpert and treatment sites were superimposed onto these maps. The data was also plotted on a line graph to generate trends over time.

Results: DR-TB case notification increased by 98% between 2010 and 2015 from 6 to 248 cases. The DR-TB treatment sites were increased by 80% from 3 to 15 and 109 GeneXpert machines were installed at 102 sites. In 2010, the first notified DR-TB patients were resident in only one district of Northern Uganda. Over the six years period there was widespread notification of DR-TB patients in 90 out of 112 districts of the country, with the highest burden in Kampala followed by Lira region. The DR-TB sites are equitably distributed in all the twelve regions of the country.

Conclusions: The detection of DR-TB in Uganda has sharply risen within six years with patients distributed across the entire country mainly resulting from expansion of GeneXpert coverage in the country.

Figure Trends of MDR-TB patients



PD-681-27 The true burden of MDR-TB in health settings in England: a focus on prevalent cases

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Background: In England, we report the number of incident MDR-TB cases notified annually. However, as many MDR-TB cases are complex to manage, and almost half have not completed treatment by 24 months, the number of incident cases does not capture the burden of MDR-TB. This analysis aims to describe the number of prevalent MDR-TB cases managed within the health services in England over a five year period, and identify factors associated with lengthy or complex management.

Methods: Notified MDR-TB cases with initial or acquired MDR-TB, or cases without culture confirmation treated for MDR-TB were included if they were prevalent in England between 2010 and 2014. Cases were considered to be prevalent between the first evidence of MDR-TB until the end of treatment.

Results: 457 MDR-TB cases were prevalent in England between 2010 and 2014. The number of prevalent MDR-TB cases was 2.5-3 times the number of incident cases reported each year, with a peak of 207 prevalent cases in 2012. The median age was 30 years, 86% were foreign born, 60% were male, and almost a fifth of cases had at least one risk factor. 52 of the 457 cases (11.4%) acquired resistance to at least one drug; 20 acquired MDR-TB and 32 MDR-TB acquired further resistance. Cases aged between 45 and 64 were more likely to acquire resistance compared to other age groups. Over 20% of UK born MDR-TB cases and 15% of Lithuanian MDR-TB cases acquired resistance compared with only 3% of Indian MDR-TB cases. Of those with 2 or more culture results, the minimum length of culture positivity was 52 days. Cases were less likely to complete treatment by 24 months if they had social risk factors, acquired drug resistance or had more severe drug resistance on their first specimen.

Conclusions: In order to plan resources and facilities to support MDR-TB patients and ensure adequate infection control, it is important to focus attention on prevalent cases. Additional support should be provided to those at risk of acquiring resistance, those at risk of lengthy TB treatment and periods of culture positivity, including those with social risk factors.

PD-682-27 Drug resistance patterns in rifampin-resistant and rifampin-susceptible tuberculosis in China

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Background: A better understanding of the proportion of rifampicin (RMP) resistance as multidrug-resistant tuberculosis (MDR-TB) and the prevalence of first line anti-tuberculosis drugs resistance in RMP susceptible TB

cases in high burden settings is urgently required to guide recommendations for treatment of TB patients. To determine the drug resistance patterns in RMP-resistant and RMP-susceptible tuberculosis in China.

Methods: Data of clinical TB strains isolated during the 2007 nationwide survey on drug-resistant tuberculosis in China and clinical TB strains from Beijing Chest Hospital during 2009-2013 were retrospectively analyzed.

Results: A total of 3929 *M. tuberculosis* strains isolated during 2007 nationwide survey on drug-resistant tuberculosis in China were included. Of the total isolates studied 88.19% (3465/3929) were RMP susceptible, and 11.81% (464/3929) were RMP resistant. Analysis of RMP susceptible strains showed resistance to at least one of the other first line drugs in 37.77% (1071/2835) and 50.79% (320/630) of isolates in new cases and previously treated cases, respectively. Analysis of RMP resistant strains showed that resistant INH is 86.63% (175/202) and 86.26% (226/262) in new cases and previously treated cases, respectively. A total of 7118 *M. tuberculosis* strains isolated from Beijing Chest Hospital during 2009-2013 were included. Of the total isolates studied 61.59% (4384/7118) were RMP susceptible and 38.41% (2734/7118) were RMP resistant. Analysis of RMP susceptible strains showed resistance to at least one of the other first line drugs in 24.2% (1061/4384) of isolates. Analysis of RMP resistant strains showed that resistant to INH is 92.47% (2528/2734). RMP-resistant/INH-susceptible isolates were significantly more likely to be susceptible to all other anti-tuberculosis drugs tested compared to MDR-TB isolates.

Conclusions: Our data suggests that among patients with a high probability of MDR-TB, RMP resistance may be a reliable proxy for MDR-TB. RMP susceptibility alone is used as an indication for first line therapy will fail to take into consideration resistance to at least one of the other first line drugs.

PD-683-27 Pattern of drug resistance among multidrug-resistant tuberculosis patients in Islamabad, Pakistan

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Background: Multidrug resistant tuberculosis (MDR-TB) is a major public health problem in Pakistan. Despite of the fact that Pakistan is amongst the top five TB high burden countries worldwide very little is known about the drug resistance patterns and dominance of multidrug resistant tuberculosis among patients from Pakistan. Now-a-days the emergence of extremely drug-resistance TB (XXDR-TB) and extensively drug resistance TB (XDR-TB) is more alarming.

Methods: This was a cross-sectional analysis. Four hundred and fifty specimens were collected from newly diagnosed MDR-TB positive patients sequentially enrolled for treatment from 2 January 2013 to 20 June 2014 in the department of pulmonology, PIMS hospital, Islamabad. Drug susceptibility testing was performed for

all 450 specimens against first and second-line anti-tuberculosis drugs. The data was analyzed with SPSS software, version 21.0.

Results: A high degree of drug resistance was observed among tuberculosis patients. Out of 450 isolates, 307 (68.2%) were resistant to rifampicin and isoniazid, 221 (49.1%) were resistant to all five first-line anti-tuberculosis drugs, while more than half (50.8%) showed resistance to second line drugs. A high proportion of samples (58.1%) were found to be resistant against ofloxacin. The major risk factors for development of MDR-TB were irrational use of anti-tuberculosis medicines and formerly treated tuberculosis patients.

Conclusions: The prevalence of MDR-TB was found to be very high in the capital of Pakistan. The high degree of resistance against second-generation fluoroquinolone (ofloxacin) is frightening. Accurately running TB control regimen with stern observation of patients ensuring completion of treatment is needed. More constricting strategies must be adapted to control non-prescription sale of ofloxacin. Physicians must be trained to avert further increase of ofloxacin resistant *M. tuberculosis* strains.

PD-684-27 Prevalence of resistance to first-line anti-tuberculosis drugs of *Mycobacterium tuberculosis* isolates in Astana city

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Background: Tuberculosis remains a serious public health problem in Kazakhstan. This study describes the distribution of *Mycobacterium tuberculosis* with first line anti-TB drug resistance in Astana city.

Methods: 600 patients were admitted to the inpatient unit of Astana TB dispensary in 2014. 296 positive culture cases drug sensitivity test to first line anti-TB drugs using the L-J proportion method and BACTEC were conducted

Results: 164 (55.4%) patients MBT were sensitive to all first line TB drugs, 132 (44.6%) MBT drug resistance (DR) was identified. 59 of DR strains (44.4%) were detected in new cases and 49 (46.2%) in relapses; other cases were generally 'interrupted treatment'. 35 patients (26.5%) had monoresistant *M. tuberculosis*, most often among patients with relapses (20; 57.1%). 54 (40.9%) patients had multidrug resistant (MDR) *M. tuberculosis*, and these were mainly new cases (24; 44.4%). Poly-resistant *M. tuberculosis* was found in 43/32.6% patients and the new cases (26-60.5%) dominated. Among patients with monoresistant cultures, 23 had Streptomycin (S), 5 Isoniazid (H) (only relapses and interrupted) and 3 Etambutol (E) resistance. 29 (58.0 %) MDR patients had resistance to 4 first line anti-TB drugs, including E, and new cases (18-36%) dominated. From patients with polyresistant cultures 12 (30.8%) had

resistance to H+S+E and most of these were also new cases. In general, among the recorded DR cases, resistance to I was most often found (99; 75.0%), resistance to Rifampicin (R) and E were less and similar, 50/37.9% and 53/40.2% respectively. New cases had 44.4% (59 from 133) DR cultures and resistance to H was fixed in most them (50; 84.7%) but to R (MDR) in 24/40.7% and to E in 26/44.1 %. Among relapses, resistance to H was found in 53.1% (29 from 49), resistance to R (MDR) in 30.1% and resistance to E was comparable to MDR (22.4%)

Conclusion: Among the new cases who had never received anti-TB drugs, a high frequency of MDR and polyresistant isolates (73.5%) were identified, which indicates features of bacillary nucleus in the population. Domination of resistance to Isoniazid calls into question not only a possibility of using it for polyresistant TB treatment of but also for chemoprophylaxis.

09. 'So sweet'? TB-diabetes screening

PD-685-27 Risk scoring system and symptom-based screening as initial steps for detecting diabetes mellitus in TB and HIV clinics in Ethiopia

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Background: Global guidelines recommend bi-directional screening for TB and diabetes mellitus (DM), but there is no well tested screening tool for resource-constrained settings to identify persons at risk of developing DM. Our objective was to evaluate the utility of a risk scoring system and symptom based screening as initial steps to identify persons at risk of DM in TB and HIV clinics.

Methods: We scored each patient using 6 criteria adapted from the published literature. Criteria included family history of DM, age, waist circumference, current smoking and alcohol use. Patients with composite scores ≥ 5 were considered at high risk of diabetes. We also administered a symptom-based checklist for acute and chronic complications of DM. Patients with at least one DM symptom were categorized as 'symptomatic'. Final diagnosis was determined by fasting plasma glucose (FPG) value of ≥ 150 mg/dl in TB patients and Random Plasma Glucose (RPG) of ≥ 200 mg/dl in HIV patients. We compared the results of risk scoring and symptom screening against the plasma glucose test. We used logistic regression analyses and Receiver Operating Characteristic (ROC) analyses to identify the predictors of abnormal plasma glucose.

Results: Of 435 TB patients, 55 (12.6%) had FPG ≥ 150 mg/dl. 38.5% and 10.1% were among symptomatic and asymptomatic patients (χ^2 28.5; $P < 0.001$). 34.8% of patients with 'high risk' scores had abnormal FPG

compared with only 11.4% in the 'low risk' group (χ^2 10.8; $P < 0.01$).

Of 2072 HIV patients with RPG, 1.5% had RPG ≥ 200 mg/dl and 2.1% were symptomatic. Of 393 HIV patients with risk scores ≥ 5 , 4.6% had DM compared with only 0.8% among those with lower risk. In multivariate analyses, having risk score ≥ 5 and being symptomatic on symptom screening were significantly associated with higher risk of DM. The ROC analysis suggested that both risk scoring and symptom-based screening can discriminate between DM and non-DM patients.

Conclusions: The risk scoring system and symptom-based checklists can be used as screening tools for prioritizing patients who need further diagnostics. Validation of these tools is needed before wider implementation in clinical settings.

PD-686-27 Active screening for diabetes mellitus among presumptive tuberculosis cases in private health care facilities, Bangladesh

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Background: The link between diabetes mellitus (DM) and tuberculosis (TB) has been recognised for centuries. In recent decades, prevalence of DM is increasing globally not only in high-income countries but also in low-income countries (LICs). On the other hand, the TB burden is already high in many of the LICs such as Bangladesh and is increasing. There is growing evidence that DM is an important risk factor for TB and might affect disease presentation and treatment response.

Methods: ICDDR, B established three Screening Centres (SCs) equipped with digital X-ray system and GeneXpert system across Dhaka city targeting the presumptive TB cases identified at the private sector. From November, 2014 to January, 2016 the SCs offered free glucometry and GeneXpert tests to the presumptive TB cases attending the SCs for chest X-ray (CXR) from the private sector. Presumptive TB cases having fasting blood sugar > 7 mmol/L and random blood sugar > 11.1 mmol/L were considered as DM.

Results: During the period 15 515 presumptive TB cases, who performed CXR were approached for DM screening. Among the approached, 3930 glucometry tests were performed at the SCs who were also tested with GeneXpert (GXP). A total of 553 (14% of 3,930) DM cases were identified and out of them 125 (23% of 553) were confirmed as TB cases, 112 (20% of 553) TB cases were positive on GXP and 13 (2% of 553) were clinically diagnosed (CD). Among the DM cases, 100 (18% of 553) were newly identified (previously unaware of their condition). Eighteen (18% of 100) TB cases were found in the group of newly identified DM.

Conclusions: The screening activities identified high rate of DM in presumptive TB cases and also high rate of TB in patients identified with DM. Screening strategies

involving both DM and TB can be considered for better understanding of the bidirectional relationship of the two diseases. Being a high burden country with TB and DM, Bangladesh can adopt such strategies to address dual epidemics.

PD-687-27 Can bi-directional screening for diabetes and tuberculosis efficiently identify cases of co-morbidity?

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Background: TANDEM is a multicentre European Commission funded study (www.tandem-fp7.eu) designed to identify optimal ways to screen and manage diabetes mellitus (DM) in TB patients. This study described the prevalence of DM among pulmonary TB (PTB) patients, and TB among those presenting with DM.

Methods: PTB patients were screened for DM in Indonesia ($n = 636$), Peru ($n = 417$), Romania ($n = 394$) and South Africa ($n = 257$). In parallel, DM patients from the same countries ($n = 809, 600, 593$ and 97 , respectively) were screened for TB. TB was defined using an algorithm including clinical symptoms, chest X-ray, culture and sputum smear test. DM was diagnosed by laboratory HbA1c ($>6.5\%$).

Results: Among 1953 TB patients, 121 cases of previously undiagnosed DM were identified (prevalence 6.5% , $95\%CI$ $5.4 - 7.6$), along with 149 cases of previously diagnosed DM (overall prevalence 14.5% , $12.9 - 16.1$). The prevalence of DM varied by age, with 34.3% and 33.9% of TB patients aged over 50 identified as DM cases in Romania and Indonesia, compared with 4.2% and 3.1% for those aged 34 or less, respectively. Overall age-adjusted DM prevalence estimates were 16.0% in Indonesia, 16.0% in Romania, 14.3% in South Africa and 10.0% in Peru. Older age, higher body mass index (BMI) and family history of DM were all associated with prevalent DM among TB patients. Overall, 14/2099 DM patients were identified as new probable/definite TB cases (prevalence 0.7% , $95\%CI$ $0.3 - 1.0$). In Indonesia there were 12 cases (prevalence 1.5% $95\%CI$ $0.8 - 2.6$). Further, 77 possible TB cases were identified in Indonesia (prevalence 9.5% ($7.6 - 11.8$)) and 5 possible cases in South Africa (prevalence 5.2% , $1.7 - 11.6$). In addition, overall 174 individuals with DM reported ever having had TB (prevalence 8.3% , $7.1 - 9.5$). Primary education only, ever smoking and lower BMI were all associated with ever having TB.

Conclusions: The high prevalence of DM justifies screening TB patients for DM, particularly those aged

over 50. However, TB seems relatively uncommon in DM patients, although the prevalence in Indonesia was higher than the general population and may be clinically important.

PD-688-27 Screening for diabetes mellitus among tuberculosis patients in Southern Nigeria: a multi-centre implementation study under programme settings

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Background: Diabetes mellitus (DM) is a known risk factor for tuberculosis (TB). In Nigeria, little is known about the burden of DM among TB patients. The WHO and The Union have called for operational and clinical research to build-up and strengthen local evidence base for action in combating the dual epidemic. The objectives of this study were; to determine 1) the prevalence of DM, 2) the additional yield of newly-diagnosed DM cases, 3) the number needed to screen (NNS) to find a new case of DM, and 4) the determinants of DM among TB patients in Nigeria.

Methods: A multi-centre cross-sectional study was conducted under programme settings in 13 health facilities in Southern Nigeria. All newly-diagnosed TB patients attending the selected health facilities between March and October 2015 were consecutively screened for DM. DM was diagnosed based on the World Health Organization criteria. A standardized proforma was used to collect socio-demographic and other clinical data. Logistic regression analysis was performed to identify factors associated with co-morbid TB and DM.

Results: Of 2094 TB patients evaluated for DM, 196 (9.4%) were found to be diabetic. Of these, 81 (3.9%) were previously known to have DM, while 115 (5.5%) were newly-diagnosed. Overall DM prevalence varied according to age group; occurring in 2.2% of patients who are 25 years or younger; and in 15.1% and 16.9% of patients in age ranges of (46-55) and (56-65) years, respectively. The additional yield of diabetes was 59% . The NNS to detect a new case of DM was 18. NNS was 119 and 9 among those aged ≤ 25 years and those aged (56-65) years, respectively. Factors associated with DM were age ≥ 40 years (aOR 2.8, $95\%CI$ 2.1 - 3.9), rural residence (aOR 2.3, 1.6 - 3.2), private facility care (aOR 2.0, 1.4 - 2.7), and having an occupation that engages in vigorous activity (aOR 0.6, 0.4 - 0.9).

Conclusions: The burden of DM among TB patients in Nigeria is high. In this and similar resource-poor settings where prioritization for DM screening is necessary; screening TB patients who are aged ≥ 40 years may yield the greatest benefits.

PD-689-27 The association between tuberculosis and diabetes: the role of glycaemic control to predict risk

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Background: The association between tuberculosis (TB) and diabetes mellitus is well established; people with diabetes are at three times greater risk of developing TB, compared to people without diabetes. While the relationship between TB and DM has been well established, the degree of TB risk based on characteristics of DM is less well known. Therefore, we sought to establish the relationship between glycaemic control and TB to determine if poor glycaemic control was associated with a higher risk of TB.

Methods: We implemented a case control study in the Republic of Kiribati (a Pacific Island nation with a high prevalence of both diseases) to assess the association between TB and DM. We recruited 275 TB cases aged 18 years and above, and 499 controls, who were adult community members without signs and symptoms of TB. Cases and controls were administered a standardised questionnaire and had height and weight measured and were administered an HbA1c.

Results: The prevalence of DM among cases was 37% ($n = 101$); among controls it was 19% ($n = 94$; $P < 0.001$). Fifty five percent ($n = 108$) of diabetes diagnoses were new. Overall, the age and sex adjusted odds ratio was 2.8 (95%CI 2.0-4.1). When assessing various levels of glycaemic control, the odds of a TB patient having diabetes increased with worsening glycaemic control. When compared to people with an HbA1c of 3-5.5% and when comparing cases and controls, the odds ratios were: 1.39 (for those with an HbA1c of 5.5-6.4%), 2.21 (for those with an HbA1c of 6.5-9.9%) and 4.85 (for those with an HbA1c of 10-17%).

Conclusions: TB risk appears to increase as glycaemic control worsens. This may have implications for screening for TB among people with DM, given that screening all people with DM may not be feasible. It also further strengthens the case for strengthening DM services at the primary care level so that patients can benefit from good glycaemic control, which has a range of benefits beyond TB.

PD-690-27 TB, HIV and diabetes mellitus tri-directional screening in four hospitals of Ethiopia

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Background: TB and HIV programs have established systems for delivering integrated services, but there is limited experience with integrated delivery of services for non-communicable diseases such as diabetes mellitus. Platforms created under TB and HIV programs may be a useful entry point for addressing the growing threat of non-communicable diseases. Our objective was to assess the feasibility and yield of tri-directional screening for TB, HIV, and DM under routine care conditions in Ethiopia.

Methods: In four secondary hospitals in Ethiopia, trained health workers from TB, HIV, and DM clinics screened patients. We used existing registers in TB and HIV clinics, new registers in DM clinics, and screening checklists, and analyzed the proportion of patients with diabetes, TB, or HIV. Fasting Plasma Glucose (FPG) ≥ 126 mg/dl in TB patients and random plasma glucose (RPG) ≥ 200 mg/dl in HIV patients were considered diagnostic of DM.

Results: Of 3439 study participants, 888 were from DM clinics, 439 from TB units, and 2112 were from HIV clinics (Table). Upon screening, six of the DM patients had TB of which five were already on treatment (overall yield of 676 per 100 000); 141 (32.4%) of 435 TB patients had FPG ≥ 126 mg/dl of which only five (3.5%) were previously detected. Of 2072 HIV patients with RPG determined, only 1.5% had RPG ≥ 200 mg/dl.

Conclusions: The yield of TB among DM patients was about three times the prevalence estimate for the general population, $>83\%$ of which were already detected by the existing system. The integrated screening approach helped detect $>95\%$ of TB patients with previously undetected abnormal blood glucose. Strengthening screening practices helps boost case detection and management both for TB and DM.

Table Yield of tri-directional screening

Screening parameters	Values
DM clinic:	
Total screened for TB	888
Number (%) diagnosed with active TB	6 (0.7)
TB clinic	
Total screened for DM	439
Number (%) with FPG ≥ 126 mg/dl	141 (32.4)
Co-infected with HIV	49 (12.5)*
HIV clinic	
Total screened for DM	2112
Number (%) with RPG ≥ 200 mg/dl	31 (1.5) †
Number (%) co-infected with TB	316 (15.8) ‡

*Of 392 HIV tested

† Data missing for 37

‡ Data missing for 114

PD-691-27 Integrating TB screening in diabetes care through Bangladesh Diabetic Samity (BADAS): moving from pilot to scale-up

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Background : Bangladesh ranks sixth among high TB burden countries, where the prevalence of DM is mounting at a dramatic rate. In 2005, the prevalence of DM in urban Bangladesh was 8%, which increased to 15% (Akter et al., 2014). Diabetes patients have a significantly augmented risk of getting active TB which is two to three folds higher than in persons without diabetes. Considering this context and after a successful pilot program from June 2013 to June 2015 under TB CARE II in tertiary level hospital (BIRDEM hospital), Challenge TB has expanded the TB screening project with Bangladesh Diabetic Samity (BADAS) from July 2015. To expand the integration of TB screening, diagnosis and referral with the existing diabetes health care services provided by one tertiary level hospital and other affiliated centers of BADAS and Bangladesh Institute of Health Science (BIHS).

Intervention or response: The project has been designed to integrate the TB services with diabetes services. National Guidelines to manage TB with DM has been developed and they provide training and orientation to health professionals to find TB cases among the DM patients. This partnership project has been supporting an integrated approach with focus on active screening of diabetic patients for detection and management of TB among them. 96 data collectors have been trained to ensure referral and recording of 17 affiliated centers and 63 local units of BADAS, as well as 9 centers of BIHS.

Results and lessons learnt: During the period of July to December 2015, a total of 7893 diabetic patients with presumptive TB have been referred by the health care workers for sputum microscopy which has increased 66% from 5195 (July to December 2014). Among them (6.8%) discovered as bacteriologically confirmed, (2.0%) clinically confirmed and (1.2%) extra pulmonary TB cases. The identification of smear positive cases has been increased by 20% during this project period from the same period of 2014 (450 to 538).

Conclusions and key recommendations: The current intervention has increased early detection and prompt management of TB among DM patients. These collaborative activities can reduce the double burden of TB-DM.

PD-692-27 Screening individuals with diabetes for latent tuberculosis infection: preliminary data from the TANDEM program in Peru

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Background: There is evidence for an increased risk of tuberculosis (TB) among persons with diabetes mellitus (DM). There is a growing burden of DM globally, particularly affecting lower income countries, where TB is also a public health problem. Peru still has a high prevalence of TB in urban areas, where DM prevalence is also increasing. There is currently no data available on the prevalence of latent tuberculosis infection (LTBI) amongst people with diabetes in Peru. TANDEM (www.tandem-fp7.eu) is a multi-country TB-DM project with field sites in Indonesia, Peru, Romania and South Africa. We present preliminary data on results of screening Peruvian DM patients for LTBI.

Methods: TANDEM DM participants were enrolled at DM outpatient facilities in a TB prevalent area in Lima-Peru, and were screened for active TB. Those with no evidence of active TB and no history of a previous TB episode were invited to be screened with the QuantiFERON-TB Gold (QFT) to determine the prevalence of LTBI. We recorded anthropometric measures and DM clinical and treatment history. QFT data collection commenced in November 2015 and is ongoing.

Results: As of February 2016, 173 patients had been recruited, the majority female (74.6%). Median age was 61 years, median Body Mass Index (BMI) was 27.7kg/m², median Waist-to-hip ratio (WHR) was 0.94 and median HbA1c was 7.9%. 41.6% of participants had been diagnosed with DM around 5 years before. 86.7% reported having received any DM treatment and among them 18.7% received insulin and 79.3% received metformin. 85 (49.1%) participants had a positive QFT result, indicative of LTBI. There was no difference in age, BMI, WHR and HbA1c between participants with positive and negative QFT results ($P > 0.1$). Neither time since DM diagnosis nor DM treatment received differed between QFT positive and QFT negative subjects ($P > 0.1$).

Conclusions: LTBI, as defined by QFT positivity, is frequent among subjects with DM in Peru. Though no clinical or epidemiological characteristics examined were associated with QFT positivity, further studies should evaluate the risk of developing active TB, comparable LTBI prevalence in an age-matched non-DM control group and cost-effectiveness of LTBI screening among this population.

PD-693-27 Prevalence of diabetes mellitus among active pulmonary tuberculosis patients in Addis Ababa, Ethiopia

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Background: The merging epidemics of tuberculosis (TB) and diabetes mellitus (DM) become major causes of morbidity and mortality throughout the world. Despite the clinical and public health significance posed by the dual burden of the two diseases worldwide, there is little evidence on the prevalence of DM among pulmonary tuberculosis patients in Ethiopia. Accordingly, the objective is devised to determine the prevalence of DM among active pulmonary tuberculosis (PTB) patients in Addis Ababa, Ethiopia.

Methods: A cross sectional study was conducted with consecutive screening of 205 active PTB cases for DM from June 2014-February 2015. Socio demographic and clinical data were collected using structured questionnaire. Cross tab, logistic regression and χ^2 test were performed using SPSS V22. $P < 0.05$ was taken as statistically significant.

Results: The overall prevalence of DM and Impaired Fasting Glucose was 8.3 % and 26%, respectively. BMI of $> 25 \text{ kg/m}^2$ ($P = 0.000$), alcohol drinking (OR 2.942, 95%CI 1.077-8.035) and smear positive PTB (OR 3.036, 95%CI 1.029-8.961) and family history of DM had a statistical association with increased occurrence of DM.

Conclusions: The present study has shown a higher prevalence of DM than the estimated prevalence in the general population. The association of sputum smear-positive TB with DM should be given special consideration for disease prevention. Further studies with a comprehensive study design are warranted to get a representative rate in TB-DM patients.

PD-694-27 Screening tuberculosis patients for diabetes in rural and urban areas of Dodoma Region, Tanzania

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Background: The growing burden of diabetes mellitus (DM) is posing a threat to global tuberculosis (TB) control. The currently ongoing demographic change in Tanzania may lead to an increase in health burden from chronic - non-communicable diseases such as diabetes. A DM screening programme in the context of TB clinics has been implemented in Dodoma region, the second poorest of the country. We report preliminary findings on the relationship between DM and TB.

Methods: All newly consecutively microscopically diagnosed TB patients ≥ 12 years at three Health Centres

from March 2015 to January 2016 were tested for DM. DM diagnostic criteria were: fasting blood glucose level (FBG) $\geq 7.0 \text{ mmol/L}$ OR random blood glucose $\geq 11.1 \text{ mmol/L}$ OR proven history of DM and of DM care OR currently receiving treatment for DM. DM diagnosis was confirmed if HbA1C $> 6.5\%$. Impaired Fasting Glucose (IFG) was diagnosed if FBG was 5.6-6.9 mmol/L.

Results: 419 TB Tanzanian patients were enrolled. Overall, DM prevalence was 2.9% (12/419). Patients living in urban areas (11/196, 5.6%) were significantly more likely to have DM when compared to those living in rural areas (1/223, 0.5%) (OR 13.3, 95%CI 1.7-103.2, $P < 0.05$). There were 4 newly diagnosed DM cases. IFG was diagnosed in 10 (2.4%) TB patients: 3 (1.5%) in urban and 7 (3%) in rural areas. TB patients were older than TB - DM patients (median 50 vs. 44), however this difference was not statistically significant. Eighty-one (19.3%) TB patients were HIV positive: of these, one was a TB-DM patient ($P < 0.001$). Rural patients were more likely to have a lower socioeconomic status ($P < 0.001$). Adjusting for age, gender, and HIV status, living in urban areas was still significantly associated with the comorbidity TB-DM ($P < 0.005$).

Conclusions: DM prevalence among TB cases was lower than reported in previous studies for other areas of Tanzania, probably related to the low economic status of the region. Nevertheless, our data confirm that patients living in urban areas are at higher DM risk compared to those living in rural areas. Finally, our results provide basal data to evaluate the cost effectiveness of this screening strategy.

PD-695-27 Study of TB diabetes collaborative activities under the Revised National TB Control Programme, Maharashtra, India

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Background: Management of co-morbidities is a part of National strategic plan implemented by National Programme. Programme has developed framework for TB-Diabetes collaborative activities in collaboration with National Programme for Prevention and control of cancer, Diabetes, cardiovascular diseases and stroke (NPCDCS). This study was undertaken with following objectives. To assess completeness of TB-Diabetes collaborative activities in Central India. To assess outcome of NSP patients with respect to diabetic status to ascertain impact of diabetes and treatment of diabetes on TB treatment outcome.

Methods: Record Review of TB patients registered in 5 districts of Maharashtra in India in year 2013. Records like Treatment card, TB register and reports like quarterly report of TB-Diabetes collaborative activities

were reviewed for the year 2013. Data entry and analysis done in Excel.

Results: 7145 TB patients were registered in 5 districts in year 2013. 1% (98) patients were known diabetic patients. 59% (4082) TB patients were screened for diabetes. 19% (784) TB patients had random blood sugar more than 110 mg/dl. 64% of 784 TB patients underwent fasting blood sugar. 136 (27%) of the patients were diagnosed as diabetic. Total 231 Diabetic patients were diagnosed in TB patients. 206 (89%) of the patients reached diabetic care. Review of treatment outcome of New smear positive TB patients who are diabetic found that conversion rate and success rate of New smear positive TB patients who are diabetic is similar to the success rate of new smear positive TB patients who are not diabetic, i.e., 88% each.

Conclusions: TB Diabetes collaborative activities have been taken up well under programme. This initiative may be expanded in entire country. High proportion of patients having random blood sugar more than 110 mg/dl suggests need of dietary and lifestyle changes in TB patients. Programme may consider its inclusion in counselling curriculum of TB patients to ensure prevention of emergence of diabetes in TB patients. Good comparable outcome in between diabetic NSP patients and non-Diabetic NSP patients draws attention importance of complete treatment of both TB and diabetes. Moreover it underlines significance of early and prompt diagnosis of diabetes in TB patients.

PD-696-27 Innovative approach to manage tuberculosis with diabetes co-morbidity in Bangladesh

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Background and challenges to implementation: Bangladesh is one of 22 high prevalence countries for tuberculosis and ranks sixth highest TB burden globally. In Asia, the prevalence of diabetes mellitus (DM) is mounting at a dramatic rate, which includes Bangladesh. Beside this, persons with diabetes have a significantly augmented risk for active TB, two to three fold higher than in persons without diabetes. Considering this context NTP Bangladesh and URC has initiated a project for exploring tuberculosis co-morbidity with diabetes mellitus with the Bangladesh Diabetic Association (BADAS).

Intervention or response: Tuberculosis comorbidity with diabetes mellitus in Bangladesh is a double burden. Currently it is a burning question both in clinical and public health aspects. In 2013, URC TB CARE II with the guidance of NTP initiated a project with Bangladesh Diabetic Association (BADAS) with the ultimate goal to address the vulnerability of the diabetic patients to acquire TB disease. The project has been designed to integrate the TB services with diabetes services and

increase access of TB services among the diabetic patients. The project developed National Guidelines to manage TB with DM, provide training and orientation to health professionals to find TB cases among the DM patients by referring TB symptomatic.

Results and lessons learnt: From July 2013 to June 2015, a total 525 Doctors, 491 nurse and 455 health workers were trained on management of TB/ DM comorbid situation. A total 13633 diabetic patients with TB symptoms have been referred by the health professional for sputum microscopy during this period. Among them 1219 detected as smear positive, 549 smear negative, 393 EP TB and 18 MDR-TB cases were detected and put on treatment successfully. The project contributed to eight-fold increase in detection of TB among the diabetes patients compared to the baseline.

Conclusions and key recommendations: TB-DM poses a potential public health challenge to Bangladesh TB control. The program is now needed good-quality implementation research for screening and to prevent and monitor this dual burden of disease.

10. Supporting MDR-TB patients: mHealth, nutrition, palliation, and health-related quality of life)

PD-697-27 Organisation of palliative care for TB patients in the Tjumen Region of Russia

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Background and challenges to implementation: Due to an increase in the numbers of socially disadvantaged patients who develop MDR/XDR-TB and stay infectious, a palliative care ward with 50 beds was established in Zavodoukovsk TB hospital in 2014. The patients have incurable TB, are suffering from alcoholism and substance abuse, unable to take care of themselves, bedridden and in need of round-the-clock care.

Intervention or response: The hospital organized a team of experts consisting of TB doctors, a psychologist, and nurses to address the palliative care needs by aiming to: provide chronic TB patients with an adequate quality of life; educate patients and their families in the basics of care; clinical follow up; and infection control. All TB patients receiving inpatient treatment were asked to complete a questionnaire aimed to identify how their quality of life in the facility could be improved. The answers were used to evaluate how many patients need assistance with activities of daily living.

Results: Six percent of patients responded that they prefer an active model of care and 94% need a passive model of care. The active model of care requires an additional individual care post to assist with activities of daily living like feeding and hygiene. The passive model of care consists of teaching patients the basics of self-care, hygiene, as well as educating them about healthy

lifestyles and diet. Applying these appropriate models of care for patients, the quality of life has improved and the patients are living longer. Socially disadvantaged incurable TB patients are discharged following treatment completion and often pass away quickly. In the new ward, patients are surviving for at least another year and longer. In addition, when adjunct and symptomatic treatment is administered, 36-38% of the patients display clinical improvement.

Conclusions: This new ward and new patient-centered approach to palliative care has improved the quality of life of incurable MDR-TB patients in the Tjumen region of Russia. However, the hospital faces challenges with implementing these models of care. There is a shortage of nursing staff and insufficient knowledge and palliative care skills among nurses.

PD-698-27 Evaluating the quality of life of MDR-TB patients in St Petersburg, Russia

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Background: Tuberculosis (TB) remains the leading cause of death due to infectious disease. Estimates show that in 2014 9.6 million people got sick with TB: 5.4 million men, 3.2 million women and 1 million children. TB as well as HIV is one of the leading causes of death worldwide. Quality of life (QoL) is a cumulative indicator reflecting a person's degree of adaptation to the disease and their chances to carry on the habitual functions corresponding to their socioeconomic status. Studying QoL gives an idea of the patient's physical, psychological and social functioning and allows us to evaluate how the patient's condition is affected by the disease. Tuberculosis as a disease lowers all health-related quality of life parameters. We aimed to evaluate the QOL of MDR-TB patients at the beginning and after three months of MDR-TB treatment.

Methods: Participants completed an anonymous self-administered SF-36 instrument. Eight quality of life parameters were assessed.

Results: A total of 34 MDR-TB patients (18 female and 16 male) participated in the study. The average age of the respondents was 38 years. At the start of TB therapy, the average physical health component was 81%, both for male and female patients, whereas the psychological health rates were 72% for male and 78% for female patients. After three months of MDR-TB treatment the physical health rate fell to 65% in male and 72% in female patients and the psychological health rate went down to 67% in the majority of the respondents. One hundred percent of the respondents experienced pain and deterioration of their social and emotional role functions after three months of MDR-TB treatment.

Conclusion: Participants reported a decrease in their quality of life while on MDR-TB treatment. It is important for health care providers to identify and manage medication side effects at early stages as well as to provide effective psychological support and facilitate successful social integration of MDR-TB patients. The

nurses should evaluate the quality of life in MDR-TB patients both at the start and during treatment to improve the patients' quality of life.

PD-699-27 Role of nutritional supplementation in treatment adherence among drug-resistant tuberculosis patients on DOTS-plus therapy in an urban slum, India

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Background and challenges to implementation: Drug resistant tuberculosis is major public health problem in India with > 65 000 cases per year. The biggest challenge faced by government authorities is high default rate (20-30%) among patients on DOTS plus therapy along with long duration of treatment.

Intervention or response: In a pilot study, patients on DOTS plus therapy were given nutritional supplements worth 15 USD per month (dry rations, i.e. pulses, ground nuts, cereals etc) during the treatment course and its effect was studied.

Results and lessons learnt: During this ongoing project, patients who received nutritional supplements at least for 6 months were analyzed. Out of 61 patients fulfilling the criteria, 28 patients (45.9%) completed the treatment during 18 months of the project. The most striking feature of this was the zero percent default rate (one patient defaulted who was later retrieved). The feedback from patients and their families was as follows: 1) reduces the indirect cost of treatment i.e. protein rich supplements; 2) Psychological support that someone care for them; 3) Eases financial burden. Provision of nutritional supplements helps in building good rapport between patient and health care provider and contributing significantly in reducing the defaulter rate.

Conclusions and key recommendations: The problem of drug resistant tuberculosis can not be solved with the current regimen due to high default rate. Providing nutritional supplements during the therapy will not only improve the nutritional status but also may reduce the default rate significantly as evident in this study.

Table Treatment outcome of patients (*n* = 61) with MDR-TB

Variable	<i>n</i>	%
Treatment completed/cured	11	18
Transfer out	3	4.9
Death	12	19.7
Failure	2	3.3

PD-700-27 Drug-resistant tuberculosis patients: they need nutritional support but acceptability matters! Lessons learnt from Mumbai, India

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Background and challenges to implementation: The association between TB and under-nutrition has long been known. Under-nutrition is a proven important risk factor and common consequence of TB. Evidence shows that the provision of nutritional support produces a modest increase in weight gain during treatment and improves treatment outcomes of TB and drug resistant tuberculosis (DR-TB). In view of the high burden of DR-TB and successful treatment outcomes of only 40% among DR-TB patients, it was been decided to provide nutritional supplements to DR-TB patients of Mumbai to improve treatment outcomes.

Intervention: The project envisaged daily provision of nutrient dense ready to cook food packet of 250 gm providing 900 Kcal. The project was piloted from February 2015 to May 2015 in Sion and Bandra wards of Mumbai covering 362 DR-TB patients. The project was evaluated in June 2015 to assess the acceptability of the supplements. Statistically significant sample size of 76 DR-TB patients was randomly selected for interview using a structured questionnaire as a part of evaluation.

Results and lessons learnt: 92% of patients were from slums or slum like areas with average per capita monthly income of 40 USD. 54% (95%CI 43%-65%) DR TB patients were underweight (BMI < 18.5 kg/m²) at the start of project. There was 58% (95%CI 46.7%-68.4%) refusal rate for nutritional supplements provided in this project. The reason being 55% patients didn't like the taste and/or smell and 23% felt it was the same kind of food daily. Refusal to consume nutritional supplement was not associated with age, sex, religion, education, working status, income, BMI or adherence to treatment.

Conclusions and key recommendations: There was felt need for nutritional support to DR-TB patients in Mumbai. Acceptability of nutritional supplementation with ready to cook food was very sensitive to taste, smell and variety. Modifications needed in food supplements provided in the project. Though little is known about most acceptable nutritional supplements for TB patients, other options like providing dry ration can be explored. National guidelines are needed to support local programs for effective implementation of such initiatives in view of issues of suitability and acceptability.

PD-701-27 Facilitators and barriers for adoption and implementation of digital health tools: a comparative analysis of 11 diverse countries

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Background: For TB program managers and health care workers alike, having access to reliable information is central to the quality of patient-centered care and program management. Particularly for MDR-TB, digital health solutions have emerged as a way to meet this need. Since 2005, a digital health solution, e-TB Manager was implemented in several countries to manage over 450 000 primarily MDR-TB patients. A multi-country comparative analysis was never performed, particularly in line with the WHO Digital Health for the END-TB Strategy's emphasis on evaluation and lessons learnt narratives.

Intervention: Data from 11 high MDR-TB burden countries that implemented e-TB Manager were analyzed. Data extraction was guided by content analysis of thematic areas for facilitators and barriers to adoption of e-TB Manager for TB program needs. This included ten key factors such as presence of local champions, political will, infrastructure, existing use and familiarity with digital health tools and data security concerns. We analyzed 82 project documents, conducted 40 key informant interviews from three high-performing countries and 12 key informant interviews with internal project staff who led the technical assistance for implementation of e-TB Manager.

Results and lessons learnt: Eight countries successfully adopted the tool to manage MDR-TB cases in country and 3 countries did not successfully adopt the tool. Selected results are presented below.

Conclusions and key recommendations: The success of digital health tools requires appropriate conditions in-country to implement successfully. Our analysis identified the need for a local champion and existing use of other digital health tools as being major facilitators to successful implementation. Barriers included strong data security concerns that slowed down or halted adoption. Countries must ensure strong leadership for successful implementation. Digital health interventions can contribute to all pillars of the End TB Strategy and improved patient outcomes.

Table Comparative analysis: facilitators and barriers

Facilitators/barriers to adoption	Implemented successfully	Not implemented
Champion	100% (8/8)	0% (0/3)
Existing use of digital health tools	75% (6/8)	33% (1/3)
Leadership (demanding use of the tool)	75% (6/8)	0% (0/3)
Data security concerns	25% (2/8)	66% (2/3)

PD-702-27 mHealth for managing MDR-TB patients at the community

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Background: Introduced through the TBCAREII project, Community based Programmatic Management of Drug Resistance TB (cPMDT) is a new strategy to improve access to and quality of MDR-TB services in Bangladesh. Providing effective care at the community level requires strong systems to ensure appropriate clinical follow-up and adherence to treatment for each patient. Considering this critical need, the project designed and implemented a mHealth application to monitor patient care and treatment adherence.

Methods: The project introduced mHealthtool in early 2013 to support the provision of home-based DOT in cPMDT area. Each MDR-TB DOT-provider was given a smartphone to assist the DOT-providers to access each patient's treatment regimen including drugs and dosing requirements. During each DOT session, the smartphone module guides the provider to record the patient's treatment history including any side-effects and perform contact tracing among family members. The Geo-tagging mechanism allows program supervisors to verify when and where each DOT session was recorded. All information of this application is stored in a central database for monitoring centrally with the coordinate point of patients' residence tagged with the record. The system allowed the project staff and government supervisors to review the updated patient records and take actions for missed DOTs, side effects and follow up issues.

Results: The mHealth application remarkably improved project-capacity for real time monitoring of DOT-providers, promoting treatment adherence, reducing missed DOT and facilitating side-effect management and follow-up. Analysis of month-wise data captured through mHealth and validated by periodic reviews of patient-cards shows 98% of the patients received daily DOT. Household visit by the DOT-providers and patient's compliance with required follow-up smear and culture tests consistently remained at 100%. Contact tracing was regularly done during the household visit and that contributed to early detection of newly infected TB and MDR-TB cases. It was also a major factor in achieving high cure rate of 84% and maintaining very low number of default cases throughout the project period.

Conclusions: Mobile phones have significant potential to facilitate case management of community-based MDR-TB patients, particularly in rural areas in Bangladesh. mHealth can play an important role to reduce burden of TB in Bangladesh.

PD-703-27 Supervision of DOT by electronic tools and cell phones can greatly improve treatment adherence of DR-TB patients

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Background and challenges to implementation: Bangladesh has adopted Community-Based Programmatic Management strategy for drug-resistant TB cases (cPMDT), which requires a strong system of follow up by community MDR-TB DOTs providers to ensure adherence for the full 20-24 months of treatment. Currently there are 95.2 million mobile phone users in Bangladesh. Given the high percentage of mobile phone users, mHealth can play a vital role in ensuring drug adherence and monitoring of DOT services.

Intervention or response: A web based smart phone application has been designed to support the provision of home-based DOT and introduced in Bangladesh in January 2013. Each MDR-TB DOT provider is provided a smartphone to assist in managing daily provision of DOT, and is able to routinely access each patient's tailored treatment regimen including drugs and dosing requirements and recording of side effects. The Geo tagging mechanism allows program supervisors to verify when and where each DOT session was recorded. All information of this application is stored in a central database for monitoring centrally with the coordinate point of patients' residence tagged with the record.

Results and lessons learnt: From January 2013 to June 2015, a total of 780 MDR-TB DOT providers were supervised by using the smart phone application covering 873 DR-TB patients in 26 districts of Bangladesh. By supervising DOT providers through mobile device, drug compliance has been increased and the regularity of the DOT providers' presence to the patients' house reached to 99%. Contact tracing through Smartphone application is contributing to active case finding of new TB and MDR-TB patients.

Conclusions and key recommendations: Mobile phones have significant potential to facilitate case management of community-based MDR-TB patients, particularly in rural areas in Bangladesh. Through active monitoring at the central level and with field level cooperation, mHealth can play an important role to ensure patient adherence to DOT and effective monitoring to reduce burden of TB in Bangladesh.

PD-704-27 The role of mHealth in the management of drug-resistant TB patients at community level in Bangladesh

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Background and challenges to implementation: Bangladesh is a high burden multi-drug resistant TB (MDR-TB) country with 4800 estimated cases (WHO Global TB Report 2015). Community-based programmatic man-

agement of drug resistant TB (cPMDT) was introduced in 2012. In 19 of the 64 districts in Bangladesh, trained DOT providers use mobile phones with an application to monitor activities and improve management of patients. At every visit to the patient, the DOT provider submits data about medication ingestion, side effects and symptomatic patient contacts. GPS geo-tracking data is automatically captured. This information is viewed and analyzed online by a district coordinator, who takes action to support the DOT provider.

Intervention or response: Methodology: To determine the benefit of mHealth, we reviewed the number of enrolled DOT providers, patients on treatment, treatment outcomes, symptomatic contacts, and side effects submitted through the mHealth application between January 2013 and February 2016.

Results and lessons learnt: 315 DOT providers used the mHealth application. The project monitored 1107 MDR-TB patients, 705 (64%) men and 402 (36%) women, using the mHealth application between January 2013 and February 2016. Currently, 453 (41%) patients remain on treatment. A total of 577 (52%) patients have been cured, 56 (5%) patients died, and 21 (2%) were lost to follow-up. 620 (56%) of the 1107 patients reported side effects. The most common side effects were: swollen feet (15%), hearing disturbance (12%), and heart burn (10%). A total of 114 symptomatic contacts were identified, of whom 96 (84%) were children. Six of these contacts were diagnosed with TB.

Conclusions and key recommendations: The mHealth application provides useful information, which can lead to better management of MDR-TB in the community setting, including management of side effects and adherence to daily treatment. However, data was not available on actions taken by DOT providers for the treatment of side effects, details on contact tracing, and the impact of the application on patient-provider interactions. mHealth has the potential to enhance the quality of care for DR-TB patients in resource-limited Bangladesh, and to serve as a vital component of patient-centered care.

PD-705-27 Using mobile health solutions to improve patient retention in Eastern Cape Province, South Africa

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Background: The increasing burden of multidrug-resistant tuberculosis (MDR-TB) in South Africa is complicated by the poor treatment outcomes in this group. South Africa has adopted decentralisation as a model for managing MDR-TB, with Eastern Cape also managing its MDR-TB patients in decentralised sites. High lost to follow up (LTFU) rates are a significant barrier to achieving improved treatment outcomes, with Nelson Mandela Bay Metro (NMBM) reporting up to 20% of

MDR patients being LTFU. A simple mHealth system was successfully introduced to geotag the DOT providers, improve the quality of DOT, and eventually, improve the treatment outcomes.

Methods: The project identified St Francis Hospice, a non-governmental organization (NGO) that provides support to MDR-TB patients in NMBM area, and enrolled the MDR-TB patients into the mHealth system. Community care givers from St Francis Hospice were trained on how to use the phone application for patient support. All patients receiving adherence support were allocated to a community care giver with their residential addresses being geo-tagged as their location of adherence support. The mHealth application guides the DOT provider in taking medical history, identifying side effects, and conducting contact tracing.

Results: Between June 2015 and February 2016, a total of 235 MDR-TB patients in both, intensive and continuous phases of treatment were enrolled into the mHealth system to monitor the DOT visits and treatment adherence. The interim data analysis shows the following results. Among the patients enrolled, only 3% reported to be lost to follow up. The patients reported as transfer-outs are those, who was re-admitted to the hospital for reasons such as severe adverse effects, worsening clinical condition and change of treatment regimen.

Conclusions: In the 9 months since introducing the mobile health application, the LTFU rates are significantly lower than the LTFU rates for the NMBM area, demonstrating a promising strategy to retain MDR-TB patients in care.

Table mHealth cohort of MDR-TB patients

Cured (%)	Lost to follow-up (%)	Died (%)	Transferred out (%)	Still on care (%)
44 (19)	7 (3)	15 (6)	44 (19)	125 (53)

PD-706-27 Impact of mHealth in increasing retention of patients in treatment

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Background: mHealth tool has been introduced to National TB Control program in January 2013 with the support of TB-CARE-II project for the management of drug-resistant TB patients in Bangladesh. mHealth application has been designed to support the provision of home-based DOT in community based MDR-TB management (cPMDT) area and to assist in managing daily provision of DOT, and is able to routinely access each patient's tailored treatment regimen. During each DOT session, the smartphone module guides the provider to record the patient's treatment history including any TB related side effects. The Geo tagging mechanism allows program supervisors to verify when and where each DOT session was recorded.

Methods: The objective of this study was to identify the impact of mHealth intervention in increasing retention of

patients in treatment. The study was conducted on the patients of quarter 1 and 2, 2013 enrolled under TB-mHealth application, in Chittagong District of Bangladesh. The number of patients included on TB-mHealth on quarter 1 was 71 and on quarter 2 was 18. At the end of the cohort, outcome reports were extracted from TB-mHealth and compared with the patients' treatment cards found at Chest Disease Hospital (CDH), Chittagong.

Results: A total of 83 patients were included to the mHealth-application between January and June 2013. Apart from the 6 patients, those were died during their treatment of MDR-TB in 1st and 2nd quarter of 2013, the rest of the 77 patients (100%) remained on treatment at the community level, including the patient was transferred out and one who had been diagnosed with XDR-TB. Smear microscopy and culture reports becomes negative by the end of 1st quarter. Previously a number of patients were reported to be dropped out from their treatment; however, from the cohort of this study, none of the patients were reported to be discontinued.

Conclusions: Mobile phones have significant potential to facilitate case management of community-based MDR-TB patients, particularly in rural areas in Bangladesh. Through active monitoring at the central level and with field level cooperation, mHealth can play an important role in reducing burden of TB in Bangladesh.

11. 'With a little help from my friends': understanding and supporting retention and adherence

PD-707-27 Perceptions and factors associated with non-adherence to tuberculosis management among patients in selected hospitals in Osun State, Nigeria

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Background: Tuberculosis (TB) is one of the greatest public health problems in the world. Non-compliance with TB management among patients has not been scientifically document in Nigeria. This study was therefore designed to patients perceptions and factors associated with non-compliance with TB Management among Patients in Osun State, Nigeria.

Methods: A cross-sectional study was conducted in all the three hospitals providing TB management in Osun State. A three-stage sampling technique was used to select 253 from the 477 TB patients who consented to participate in the study. Data were collected using a semi-structured questionnaire. Perceptions of TB were determined using a 12-point perception scale. A positive perception attracted a score of 2 points while the score for a negative perception was zero. A total score of < 12 and ≥ 12 points were considered negative and positive perception respectively. The data were analyzed using descriptive statistics and χ^2 .

Results: Mean age of respondents was 47.4 ± 6.2 years and 83.5% were males. Many (36.8%) had either Ordinary National Diploma (OND) or National Certificate of Education (NCE) and 34.5% had Secondary School Certificate (SSC). Respondents mean perception score was 10.6 ± 4.4 . Many (78.9%) of the respondents had a negative perception while 21.1% had a positive perception. The perception of (54.5%) of the respondents' was that TB cannot be cured completely with western medicine and 32.4% were of the opinion that the cause of TB is spiritual. Most (56.4%) were of the perception that TB cannot be prevented because is airborne disease and 15.9% believed that over-crowding is not a risk factor for TB. The mean perception scores of respondents with first degree, OND/NCE and SSC were 10.6, 9.9 and 9.4 points respectively ($P < 0.05$). Respondents' reported factors associated with non compliance with TB management included stigmatization (93.9%), continuous use of drug for long time (78.9%), negative attitude of health workers (40.8%) and forgetting to use drugs as prescribed by the doctor (34.8%).

Conclusion: Negative perceptions of tuberculosis existed among the respondents. Information, education and communication programme on tuberculosis management should be intensified for the respondents' by government and non-governmental organizations

PD-708-27 Reasons for pretreatment loss to follow-up of tuberculosis patients in Chennai, India: a qualitative study

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Background: Prior local studies have reported that 5 to 22% of patients diagnosed with smear-positive TB in India's Revised National Tuberculosis Control Programme (RNTCP) fail to initiate TB treatment—a problem referred to as pretreatment loss to follow-up (PTLFU). National data from the RNTCP suggest that 10-12% of diagnosed smear-positive patients are unaccounted for and likely PTLFU cases. None of the prior local studies conducted in-depth interviews with PTLFU patients; therefore, there is a dearth of information on the reasons for PTLFU from the patients perspective.

Methodology: We report data from an ongoing cross-sectional study aimed at identifying the prevalence of, and reasons for, PTLFU in Chennai. From November 2015 to January 2016, we tracked smear positive patients at 18 designated microscopy centres with the help of RNTCP healthcare providers. PTLFU was defined as failure to enroll in treatment within two weeks of diagnosis. In-depth qualitative interviews were conducted with all PTLFU cases after informed consent to elicit reasons for failing to initiate treatment. The

interviews were audio taped, transcribed and content analysis was used to identify themes.

Results: Of 276 smear-positive patients diagnosed, 14 (5.1%) were PTLFU within two weeks of diagnosis. Individual-level factors expressed by patients included inconveniences with the treatment centre the patient was referred to, delays in the referral process and lack of information on the need to collect their results and the adverse effects of not initiating treatment. Some patients had heard from other patients on the side effects of drugs and therefore not initiated treatment. Excessive alcohol intake was a barrier that prevented male patients initiating treatment. Other reasons included family commitments, financial constraints due to loss of wages every time they visited the health centre.

Conclusion: Our preliminary findings highlight that PTLFU continues to remain a challenge to TB control. Central to many of the reasons for PTLFU is lack of adequate counseling of patients—especially with regard to the fact that they have been diagnosed with TB, referral directions to reach treatment sites, and medication side effects. A patient-centered approach with enhanced counseling may help to reduce PTLFU in the RNTCP.

PD-709-27 Profile of patients dropping out of TB treatment, Brazil, 2013

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Background: One of the most challenging aspects in the current scenario of the fight against tuberculosis is the abandonment of treatment. Abandonment of drug resistant tuberculosis cases (TB-DR) is even more worrying, because it can increase the incidence of primary resistance and the mortality. The aim of this study is to describe the profile of TB-DR patients that abandoned treatment in Brazil in 2013

Methods: it is a descriptive study of TB-DR patients dropout in Brazil in 2013. The cases of TB-DR are of mandatory notification and must be reported on the information system for special treatment of tuberculosis (SITETB). The variables analyzed were based on sociodemographic profile (gender, age, race, education), type of resistance (primary or acquired), standard resistance, number of previous treatments, associated comorbidities and conducting DOT

Results: In 2013 were registered 727 cases of TB-DR in SITE-TB, of these 144 (20%) were lost to follow up treatment. Of the total number of abandonment, 75% were male, 30% were between 35 and 44 years, 42% were mixed race, 45% had 4-7 years of study. Acquired resistance was 83%, 69% were multidrug-resistant (resistance to at least rifampicin and isoniazid), 41% had one previous treatment. Of the associated comorbidities, 28% reported to be users of some illegal drug and 35% were alcoholics. DOTS was performed in 77% of cases.

Conclusions: There was a high percentage of lost of follow up in cases of TB-DR. This occurrence was higher among men, with considerable percentage of illicit drug users and alcohol abuse. This large percentage of abandonment in this population is worrying, thinking in the difficulties of treatment and disease control. Although most cases be treated with DOTS, the observed data show the need to improve the quality of this treatment and to develop new strategies for increase the adherence to the treatment of the patients with resistant TB.

PD-710-27 Association between counselling and adherence to treatment for MDR-TB patients in two districts of West Bengal, India

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Background: Treatment for sensitive tuberculosis (TB) is easier compared to Multidrug-resistant TB (MDR-TB). Patients are often despondent due to failed previous treatments, difficult regime of 24 months+ with daily injectable drugs. Other programmes like HIV/AIDS have embedded counseling to improve compliance to similar difficult and protracted treatment regimens. Hence, a CARE India-supported psychosocial counseling project, in collaboration with National TB programme of India was initiated in two districts of West Bengal for facilitating treatment compliance among out-patient MDR-TB patients. We aimed to assess whether increasing frequency of counseling sessions was associated with improved treatment outcomes in MDR-TB patients.

Methods: Programmatic Management of Drug Resistant TB (PMDT) data of all the patients who started treatment between January 2013 and June 2014 were analyzed from Bardhaman and Howrah districts of West Bengal. Each patient was assigned a total score by adding their individual monthly counseling scores over a 12-month period from treatment initiation. In Bardhaman, they were administered through personal meetings, telephonically or absentee visits, which were assigned a score of 1, 2 and 3 respectively. For Howrah it was 0 and 1: not counseled or counseled. The individual composite scores were tertiled into low, intermediate and high. The outcome variable was sputum results at 12 months: negative, positive/dead or others; dichotomized into negative and others for logistic regression.

Results: A total of 316 and 309 MDR-TB patients with median ages 32 and 27 and predominantly males were administered counseling from Bardhaman and Howrah respectively. 70% and 82% of them in the highest score tertile in Bardhaman and Howrah respectively had negative results as compared to 61% and 26% with least favourable results from lowest score tertile ($P < 0.001$). The Odds Ratio of getting a negative result was 5.09 times (2.24-13.18) and 5.97 times (3.29-11.12) in highest score tertile for Howrah and Bardhaman respectively. After adjusting for caste and income discrepancy for Bardhaman, the OR is partially attenu-

ated to 3.53(1.88-6.80), while no adjustment could be done for Howrah.

Conclusions: Increased counseling of MDR-TB patients is associated with improved intermediate treatment outcomes.

Figure Association between counseling/outcome, A) Bardhaman, B) Howrah

Annual score (Tertiles)	Intermediate treatment outcomes, Bardhaman N(%)		
	Negative	Others	Positive/dead
Lowest	36(27.3)	15(11.4)	81(61.4)
Intermediate	62(63.3)	14(14.3)	22(22.4)
Highest	56(69.1)	16(19.8)	9(11.1)

Annual score (Tertiles)	Intermediate treatment outcomes, Howrah N(%)		
	Negative	Others	Positive/dead
Lowest	78(47.3)	45(27.3)	42(25.5)
Intermediate	43(58.1)	28(37.8)	3(4.1)
Highest	32(82.1)	5(12.8)	2(5.1)

PD-711-27 Association between tuberculosis-related stigma and medication adherence among TB patients in China

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Background: China has one of the highest tuberculosis (TB) and multidrug-resistant TB (MDR-TB) burdens globally. Stigma is reported to be a major factor affecting patient treatment adherence. Different social and cultural backgrounds may influence different levels and perceptions of stigma among patients. We aimed to describe the status of tuberculosis-related stigma in Chinese TB patients; and (2) to explore the association between tuberculosis-related stigma and medication adherence in Chinese TB patients.

Methods: A cross-sectional study was conducted at the Beijing Chest Hospital, China. A convenience sample of 120 TB patients was recruited. Data were collected from April 2015 to December 2015 in inpatient and outpatient departments. The Tuberculosis-related Stigma Scale (TSS) with two subscales was used to measure stigma of the participants, and the Morisky Medication Adherence Scale (MMAS) 8 items version was used to measure participants' medication adherence.

Results: The average scores (standard score) of the two subscales of TSS were 27.71 9.51 (community perspectives) and 25.73 8.65 (patient perspectives), respectively. A higher score on the TSS indicates a greater perception of stigma. The scores of patient perspectives subscale of stigma had correlation with their scores of medication adherence measured by MMAS ($r=0.21$, $P < 0.05$). The participants were grouped as high, medium and low adherence according to their scores measured by MMAS. The mean scores (mean \pm SD) of the patient perspectives subscale of stigma by three adherence stages were 21.02 4.81, 25.68 7.75, and 27.03 9.78 respectively. This indicates that patients with a higher TSS score had lower treatment adherence. Significant differences were found among patients with different adherence stages ($F = 2.96$, $P = 0.05$). There were no significant differences in the mean scores of the community perspectives subscale among patients with varied levels of adherence ($F = 1.33$, $P = 0.27$).

Conclusion: Chinese TB patients experienced different levels of tuberculosis-related stigma; patients who had lower treatment adherence experienced higher level of perceived stigma. Further study is suggested to be conducted in a larger sample. There is a need for improved community awareness and education to reduce stigma towards patients with TB.

PD-712-27 Will an early counselling intervention with treatment interrupters help to prevent loss to follow-up among drug-resistant TB patients?

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Background and challenges to implementation: India accounts for 64 000 DR-TB cases accounting for 22% of global burden. Approximately 20% of the patients are lost to treatment and its one of the challenges in tackling DR-TB. National Strategic Plan 2012-2017 focuses to improve the treatment outcomes of DR-TB patients by preventing loss to follow up and ensuring treatment compliance among DR-TB patients.

Intervention or response: Since April 2014, Population Services International (PSI) in collaboration with RNTCP piloted psychosocial counselling intervention across 28 districts in India. Professional counsellors with master's degree in social work, sociology or psychology were recruited and trained in counselling of DR-TB patients. The key roles of DR-TB Counsellors include providing facility and home based counselling to all DR TB patients currently on treatment with an objective to prevent loss to follow up, ensure adherence and treatment completion. The counsellors identify treatment interrupters within 7 missed doses by liaising with DOTS providers, make home visits to address causes for treatment interruption such as side effects, psychosocial, family issues to ensure that the patients are retrieved

back on treatment and future loss to follow up is prevented.

Results and lessons learnt: During May 2014 to December 2015 more than 3065 on treatment patients were counselled in own districts. 398 DR-TB patients (308 male, 90 female) were reported Treatment Interrupters during intervention period. Out of these counsellors actively tracked 385 (299 male, 86 female) were counselled. 73% of treatment interrupters were retrieved back on treatment within 15-20 days of interruption. Empathetic counselling, regular follow-up, catalysing family and social support helped to bring these patients back on treatment. As a result of early intervention with treatment interrupters only 6% of MDR-TB patients were loss to follow up (LTFU) in the intervention districts as compared to 18% Loss to follow up (LTFU) in pre-intervention period.

Conclusions and key recommendations: Early tracking of patients to identify treatment interrupters, empathetic counselling, regular follow up, facilitating family and social support and DR patient helps to prevent overall loss to follow up among DR-TB patients.

PD-713-27 Patient-centred treatment support groups: the final solution to end loss to follow-up in tuberculosis

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Background and challenges to implementation: Morbidity, catastrophic expenditures, difficult access, social stigma and confidentiality issues weave a tricky web around the sick TB patient. Direct Observation of Treatment (DOT) alone has not resulted in 100% adherence to treatment. Significant proportion of patients are lost to follow up even in good DOT settings. Adherence to TB treatment is important in preventing relapse and emergence of resistance. Pathanamthitta district in South India is implementing Revised National Tuberculosis Control Program (RNTCP) since 1993. The district program was reporting approximately 5% of their diagnosed sputum smear positive pulmonary tuberculosis patients as never put on treatment (Initial loss to follow up - ILFU) and 5% of the New Smear Positive Pulmonary (NSP) TB patients as lost to follow up (LFU) during treatment. Attempts based on DOTS were not largely successful in bringing down these proportions further.

Intervention or response: A treatment support group [TSG] is a non-statutory body of socially responsible citizens and volunteers to provide social support to each needy TB patient safeguarding his dignity and confidentiality by ensuring access to information, free and quality services and social welfare programs, empowering the patient for making decision to complete treatment successfully. The group is usually chaired by the president of Gram Panchayat (the lowest tier of local self-

government) or a local opinion leader. Members are, Medical Officer, peripheral health worker, community DOT provider, experienced informal counsellors, members of community based or faith based organizations and local philanthropists. It is complete fulfilment of social inclusion standards enumerated by Standards for TB Care in India. Pathanamthitta district started implementing TSG strategy since 2013.

Results and lessons learnt: After intervention, proportion of LFU among NSPTB cases dropped markedly and no LFU were reported among the latest treatment cohorts from 2014. Proportion of ILFU keeps similar trend and none were reported among the latest diagnostic cohorts from 2014.

Conclusions and key recommendations: Social support for TB care is feasible under routine program conditions. The model does not burden the health system for additional resources. With TSG strategy, lost-to-follow-up of tuberculosis patients is completely preventable.

PD-714-27 Kyrgyzstan food parcels distribution practice and its influence on strengthening patients' adherence to treatment

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Background and challenges to implementation: Project HOPE Kyrgyzstan, principle recipient of the Global Fund Round 9 TB program, developed and implemented a food parcel (FP) distribution program for TB patients on the continuation phase of treatment with the objective of increasing patient's adherence to TB treatment.

Intervention or response: A comprehensive system of FP distribution was developed which included all required recording and reporting documents, agreements, procurement processes, delivery, inventory control and storage, product quality and its distribution according to schedule. The system was deliberately designed to distribute the FPs in the places where patients normally get their TB medication. This enables the staff to integrate with primary care and TB services, which helps minimize the number of staff needed to run the program and helps ensure patient monitoring and coordination with services. During FP distribution, all patients received information sessions on TB and the opportunity to discuss their health and adherence issues with health care workers. Since a high number of patients did not have their sputum check as scheduled during their 5th month of treatment, the sputum check was included as a condition to receive a FP.

Results and lessons learnt: Overall in 2015 the absolute number of patients participating in the food distribution program was 4826 of the 7058 patients on treatment. Analysis of the data on 4826 of TB patients in all regions of Kyrgyzstan from January 2015 to December 2015 showed that 99% of TB patients enrolled in the FP distribution program came for their X-ray examination and sputum check as scheduled at 5 months compared

with 73% among TB patients who didn't participate in program

Conclusions and key recommendations: Integration and coordination of the FPs with primary care and TB services, combined with the additional motivating incentive of the FPs, makes it easier for patients to comply with adherence. With a 99% compliance rate, it is recommended that this strategy be replicated to ensure greater patient adherence to TB treatment.

PD-715-27 Development and implementation of an approach to providing support for patients within Nepal's MDR-TB management programme

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Background: Emergence of MDR-TB is continuous threat for the success of the National TB Programme (NTP) in Nepal and many developing countries. Limited numbers of treatment centres means patients need to live away from home for treatment that commonly lasts 20 months but sometimes as long as 24 months. This, coupled with stigma and discrimination associated with TB, and the psychological effects of MDR-TB drugs, seriously affect psychosocial wellbeing of MDR-TB patients.

Patient support is one of the strategic components of the END TB Strategy. Despite the wide acknowledgement of the impact of treatment on patients' psychosocial wellbeing, existing TB care focuses primarily on medical aspects of the disease.

Intervention Health Research and Social Development Forum (HERD), in collaboration with the Nepal National Tuberculosis Centre, have developed a patient support approach appropriate for local context. The intervention is based on the Healthy Activity Programme (HAP) model and aims to reduce psychosocial burden of the patients and their family members during treatment. The intervention uses screening tools to identify patients with depression; psychosocial counselling support is tailored to patient needs, particularly in terms of the level of social isolation, depression and anxiety experienced by patients.

Lessons learnt: Provision of psychosocial support by counsellors using HAP model is reported to be acceptable, relevant and beneficial in reducing MDR-TB patients' psychosocial problems. However, such interventions must take into account health-workers' time availability and the specific skills set required in order to institutionalize and scale up such interventions and integrate them into regular service delivery mechanisms. Providers welcomed provision of counselling as an opportunity to provide a comprehensive service to the

patients; but very few patients met the criteria of receiving the intervention, contrasting with providers' perceptions of need, indicating the need to build capacity of health workers to better identify depression amongst MDR-TB patients. To ensure effectiveness, scalability and sustainability, such interventions need to be embedded in the routine healthcare system.

Conclusion: Psychosocial support appears to be effective to support MDR-TB patients and reduce psychosocial issues, but interventions must be designed in ways that can be integrated into the regular health care system.

PD-716-27 Effect of a social support package on treatment adherence of DR-TB patients in Bangladesh

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Background and challenges to implementation: Non-adherence to Drug Resistant Tuberculosis (DR-TB) treatment jeopardizes patient wellbeing and adversely affects TB control. Provision of social support to patients and DOT providers during treatment can be a significant motivator. In 2012 the National TB Control Programme (NTP), Bangladesh adopted community-based programmatic management of a DR-TB (cPMDT) policy to shorten long hospital stays and decrease waiting time for new patient enrolment. The policy allows early release and treatment in the patients' own communities. Considering the demand for close monitoring and common barriers to treatment adherence, NTP also introduced a social support package for enrolled DR-TB patients and their DOT providers in mid-2012.

Objectives: To assess the effect of the Social Support Model on treatment adherence and outcomes.

Intervention or response: Since July 2015, the Challenge TB project (CTB) has provided a social support package that includes monthly monetary support for: 1) nutrition of patients; 2) baseline and monitoring of ancillary investigations such as X-rays, renal tests, and liver function tests; 3) travel allowance for patients to submit samples; 4) courier service for follow-up sputum transportation and early delivery of follow-up culture reports; 5) DOT provider incentives; and 6) DOT provider travel costs to collect second-line drugs. CTB Bangladesh provides a drug box, bag, umbrella, and flashlight for DOT providers, who are community health workers or community volunteers.

Results and lessons learnt: Maintaining DOT providers' commitment and effectiveness for better services to patients is a challenge. Social support contributed to high rates of treatment continuation and success.

Prevention of misuse is ensured through vigilant supervision as well as utilization of an electronic mobile phone-based system of disbursement.

Conclusions and key recommendations: Provision of the Social Support Model has maintained low loss to follow up rates that ultimately lead to higher treatment success rates through enhancing treatment adherence at community level.

Table DR-TB patient management status as of 29 February 2016

Year	Enrolled	Treatment Success %	Lost to follow-up %	Still on treatment %
2013	341	87	3.5	Not applicable
2014	458	32	5.45	51
2015	443	Not applicable	3.16	87

PD-717-27 The use of community health workers in the in-patient setting to improve TB treatment outcomes in Karasburg, Southern Namibia

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Background and challenges to implementation: Karasburg is a remote district in Southern Namibia, with a TB case notification rate (CNR) of 618/100 000 (2014) and population density of 0.4/km². The district has severe nursing staff shortages, with overworked nurses developing negative attitudes and low confidence towards TB management. In-service training offered locally was generally ineffective, and there were limited resources for comprehensive external training. The TB lost to follow up (LTFU) rate was as high as 8% per year for new smear positive (NSP) cases and 21% for retreatment cases. In 2013, community health workers locally known as TB Field Promoters (TB-FPs) were redeployed to cover inpatient settings.

Intervention or response: TB-FPs were assigned on a daily rotational basis to the TB Ward to work with nurses. Their role includes DOT, managing sputum collection and results, daily health education, nutritional management, contact tracing, adherence support and discharge planning for TB patients. This approach recognizes the strength and commitment of TB-FPs to improve case management from diagnosis while in hospital to completion of treatment as outpatients.

Results and lessons learnt: This initiative resulted in an improved treatment success rate (TSR) from 79% for NSP cases in 2010 to 88% in 2014. Among retreatment cases the TSR rose from 70% in 2010 to 86% in 2014. LTFU dropped from 5% in 2010 for NSP cases to 0% in 2014, while among retreatment cases it dropped from 21% in 2011 to 0% in 2014. There is a higher index of suspicion for TB in the community, increased awareness and better educated patients. Treatment supporters act promptly on indications of potential interruption. There is increased confidence and reduced stigmatization of TB patients by nurses.

Conclusions and key recommendations: Usage of FPs in the hospital setting alleviated the burden of nurses and assisted in shifting tasks, showing positive treatment outcomes. Sharing workload with a common goal contributed to improved staff morale, improved team work and improved TB treatment outcomes. The role of FPs in TB wards should be reviewed and strengthened to include holistic approach to case management from diagnosis to completion of treatment.

PD-718-27 Pharmacists and rural health care providers as key players in the fight against MDR-TB: experiences from the PRATAM Project, India

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Background: TB Alert India is working with Pharmacists and Rural Health Care Providers (RHCPs) since last three years in Telangana state, India. Objective of the project is to bring in their active engagement in TB Care and control. Project is being supported by Lilly MDR-TB Partnership. Pharmacists and RHCPs are expected to refer people coming to them for cough treatment to TB testing. From Feb 2013 to December 2015, pharmacists/RHCPs have facilitated testing of 5735 people with TB like symptoms. Around 702 (12%) among tested are diagnosed with TB. Referring for testing will be one time job, but DOTS provision involves regular follow up and is time consuming. The project wanted to evaluate whether Pharmacists and RHCPs can be good DOTS providers.

Intervention: Pharmacists/RHCPs were explained the role they could play as DOTS providers. They were encouraged to take up DOTS provision. Project established linkages between pharmacist /RHCPs and local National TB Program (NTP) officials responsible for treatment. All the willing pharmacist/RHCPs were listed as DOTS Providers in local NTP records. Near about 73 TB patients were allotted to project enrolled pharmacist / RHCPs for DOTS provision in span on 18 months.

Results and lessons learnt: Among 73 TB patients taking treatment at pharmacists/RHCPs, 84% (61/73) are declared cured /completed treatment. Only 3 (4%) TB patients have been lost follow up to treatment. Around 5% (4/73) died within one to two months of treatment initiation. One patient each have been transferred out and converted to MDR treatment. Remaining 3 TB patients are still on treatment. These findings are more or less in line with the country NTP guidelines. In spite of wide spread belief that pharmacists/RHCPs are too busy and business oriented, contribution of pharmacists/RHCPs is very encouraging. This is both in terms of early identification of TB patients and in ensuring treatment completion. Close follow up and continuous motivation are the key aspects in engagement of pharmacists/RHCPs.

Conclusions: Pharmacists/RHCPs are real assets who are widely spread at community level, on whom NTP can bank on for better treatment outcomes.

12. TB transmission

PD-719-27 Findings from tuberculosis investigations associated with air travel, Canada, 2008-2012

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Background: The Public Health Agency of Canada (PHAC) coordinates the Tuberculosis and Air Travel activity (TBAT), whereby provincial and territorial public health authorities (i.e., reporting jurisdictions) report to PHAC on persons diagnosed with active tuberculosis (TB) who travelled on commercial aircraft, for the purpose of conducting contact investigations. PHAC also receives outcome information on passenger contacts, as available.

Methods: TBAT administrative data were analysed to examine trends in reporting patterns and risk of TB transmission between cases and passenger contacts during air travel for all TB index cases reported to PHAC from 2008 to 2012. Descriptive statistics are presented. Risk of TB transmission was estimated using the number of passenger contacts with positive test results (i.e., tuberculin skin test, Interferon Gamma Release Assay) among those who had a medical assessment.

Results: There were 357 TB index cases reported from 2008 to 2012, of whom 160 (45%) met the Canadian criteria for initiating a contact investigation. 6275 passenger contacts were identified, including 5713 (91%) with sufficient contact information (i.e., complete mailing address) to allow for a contact investigation. Jurisdictions reported outcomes for 1085 (19%) passenger contacts; of those, 701 (65%) were reached, including 653 (93%) for whom test results were received. Among the 653 medically assessed passenger contacts, no cases of active TB were reported; among the 78 LTBI cases, 4 were newly diagnosed LTBI but with no known previous risk factors. Estimated risk of TB transmission ranged from 4 passengers (i.e., those passengers with positive test results and no known previous TB risk factors) to 190 passengers (i.e., all passengers with positive test results regardless of TB risk factor history) (0.6%-29.1%).

Conclusions: This analysis was not able to demonstrate clear evidence of TB transmission between index cases and passenger contacts during air travel; however, the estimated risk results indicate that there may still be a non-zero risk of transmission via aircraft. These results echo those of other analyses indicating inconclusive evidence of TB transmission during air travel. Future assessments could consider analysis of additional out-

come data and explore the use of genotyping to determine transmission patterns.

PD-720-27 Real time investigation of tuberculosis transmission: technical progress in the SAMRC and Gates Foundation Aerobiology of TB Studies

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Background: We identified tuberculosis (TB) transmission as an important but under-studied area of research and thus assembled a multidisciplinary team to systematically address bacterial, host and environmental factors contributing to TB transmission in a high-burdened target community.

Methods: Two sampling systems were constructed that allowed sampling of particles released from untreated patients actively infected with drug sensitive pulmonary tuberculosis (PTB) and TB screen-negative volunteers. One system simulated a room environment with released respiratory particles being allowed to age prior to sampling while the second system aimed to efficiently capture aerosol particles soon after release from the participant. Participant carbon dioxide production, particle size distribution, fluorescence characterisation, depolarisation investigation, electron microscopy, mass spectrometry, droplet digital PCR and culturability of airborne TB bacilli platforms were developed, tested and optimised for these two sampling systems.

Results: We will discuss the challenges and innovations developed in the project along with the measured efficiencies achieved in the sampling. Intellectual contribution from a wide array of people, built a sampling system that capable of characterising cough aerosol production from a wide range of viewpoints. Data from controlled release of particles and model organisms will be compared to data collected from participant samples.

Conclusions: The complexity of airborne biological sampling has been revealed and the first period of this project has allowed the multidisciplinary team to establish as effective and well characterised sampling system.

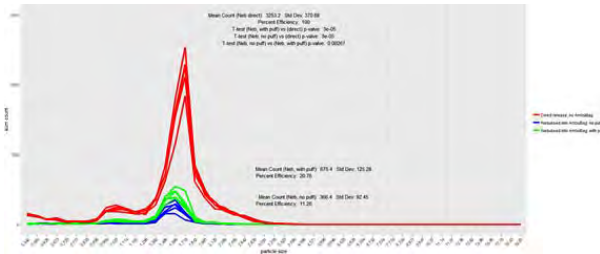


Figure Example of particle size range of a standardised cough compared to direct particle release using standard 2 µm spheres suspended in water. Three methods of release were compared; direct nebulising into the capture chamber, actively forcing and passively bleeding particles into the chamber using an ambubag. Using tests such as this we are able to ascertain system losses and improved sampling efficiencies through adapting the sampling system design.

PD-721-27 A novel approach in identifying tuberculosis transmission hotspots in urban Tanzania by using carbon dioxide levels and social information

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Background: The ambitious global tuberculosis (TB) control targets require novel approaches to study transmission and develop appropriate intervention strategies. Indoor carbon dioxide (CO₂) concentration levels have been previously suggested as a proxy for estimating airborne transmission potential. We determined the infrastructure-related TB transmission potential in locations of public importance by combining CO₂ measurements with social contact information.

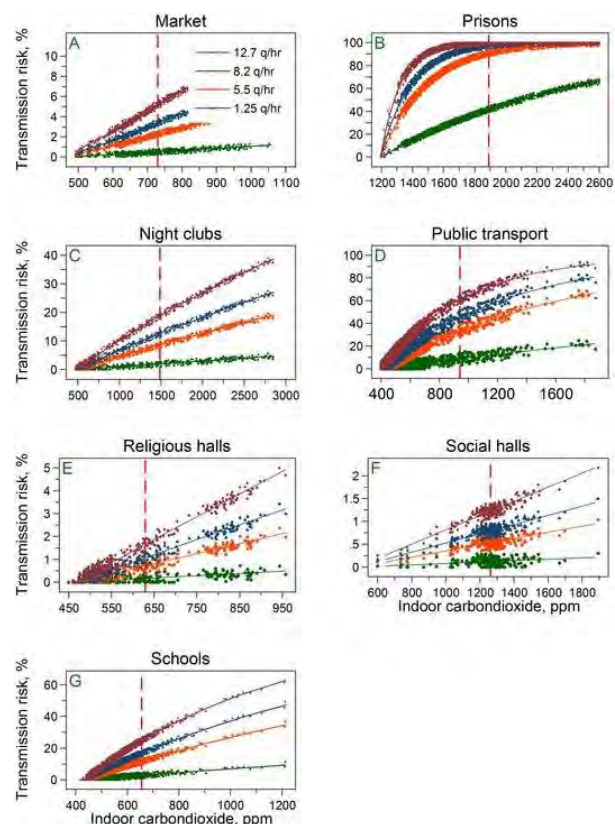
Methods: We collected environmental CO₂ levels from markets, prisons, night clubs, public buses, religious halls (churches and mosques), schools and social halls using adult volunteers. All study volunteers recorded the time spent at each location and the number of people present. We calculated the mean indoor CO₂ levels and volumes of re-breathed shared air at each location. We used a simple mathematical model (modified Wells-Riley equation) to estimate the annual risk of TB transmission assuming a quanta of contagion of 1.25/hour and a TB prevalence of 295/100 000 population.

Results: The estimated annual risk of TB transmission was highest at prisons (41.6%), followed by public transportation (4.5%), night clubs (1.7%), schools (1.48%), indoor markets (0.48%), religious (0.17%) and social halls (0.12%) (Figure). The annual risk of TB transmission in markets was higher among traders compared to customers (mean 4.9%, 95% confidence

interval [CI] 4.77-5.05 vs. 0.49%, 95%CI 0.48-0.51 $P < 0.001$). The mean annual transmission risk for a driver in public transport was higher compared to a passenger (20.3%, 95%CI 20.04-20.53 vs. 2.36%, 95%CI 2.33-2.39, $P < 0.001$).

Conclusions: We estimated the highest annual TB transmission risk in prisons, followed by public transportation, night clubs, schools and indoor markets. Locations such as religious and social halls appear to play a minor role in transmission. Interventions such as improving ventilation conditions at the transmission high-risk locations should be considered to control TB.

Figure TB transmission risks at locations of public importance in Tanzania.



PD-722-27 Dynamics of tuberculosis transmission in an Italian metropolitan area

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Background: Italy is a tuberculosis (TB) low incidence country, though Rome shows, as most other metropolitan European cities, TB incidence rates higher than Italy as a whole, with patients of many nationalities, making it an ideal place to investigate the modern trends in TB in

Western Europe. The presence of *M. tuberculosis* strains belonging to different phylogeographic lineages and showing different drug susceptibility patterns indicates a high genetic variability, with implications in terms of patient clinical management and disease control. The aim of this study was to carry out an epidemiological investigation of the TB cases in Rome by collecting classical and molecular data, in order to characterize the TB epidemic dynamics in a metropolitan area and to improve control measures.

Methods: A total of 232 isolates, collected from new or previously treated patients, admitted between 2008 and 2014 at two hospital settings in Rome with diagnosis of TB, were analyzed by Spoligotyping and 24 loci MIRU-VNTR. SITVIT2 database and the MIRU-VNTRplus web application were used to identify the strain genotypes and to generate phylogenetic trees.

Results: Two-hundred-thirty-two TB strains (70% from foreign born patients) were genotyped by MIRU-VNTR and Spoligotyping, and an UPGMA phylogenetic tree was generated based on their lineage. The Euro-American lineage, as expected, was the mostly present (81.9%) within both, Italian and foreign born population, although all main lineages are represented. Strains were further defined by their sublineage, and several clusters were identified. Molecular epidemiology results were then linked to classical epidemiology and with clinical and microbiological data, showing similar drug susceptibility patterns and correlations with country of origin within the clusters.

Conclusions: Dynamics of TB transmission in Rome highlights the presence of *M. tuberculosis* lineages and clades that reflect the patients' country of origin. Knowledge from molecular and classical epidemiology provides important tools for early identification of clusters of tuberculosis transmission, bringing to a better disease control.

PD-723-27 Long-term observation of molecular epidemiology of *Mycobacterium tuberculosis* in an urban area in Japan

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Objective: To evaluate the status of transmission of *M. tuberculosis* and socio-demographic factors with genotype clustering in Shinjuku City, Tokyo, Japan, using epidemiologic and genotype data collected over a period of ten years.

Methods: Demographic and clinical information, and IS6110-RFLP patterns of *M. tuberculosis* of bacillus-positive tuberculosis (TB) patients notified to Shinjuku City between 2002 and 2012 were collected and analyzed. We classified participants to 'genotype cluster', defined as more than 2 isolates with more than 6 IS6110 bands with identical band patterns or with < 6 IS6110 bands with identical band patterns and confirmed by identical spoligotyping, and to 'non-genotype cluster',

defined as those other than above defined patients. Multivariate logistic regression was used to calculate adjusted odds ratio (AOR) of genotype clustering after controlling simultaneously for potential confounder variables.

Results: Of a total 1018 TB patients analyzed, 611 (60.0%) were smear positive pulmonary TB, 327 (32.1%) were smear negative pulmonary TB, and 80 (7.9%) were extra-pulmonary TB. A total of 105 genotype clusters consisting of 494 TB patients were identified; the average size of a genotype cluster was 4.7 and genotype clustering rate was 38.2%. Patients belonging to the largest cluster ($n = 29$) have notified over long time period (2003-2012). Of the 29 patients, 27 (93%) were < 65 year-old and 16 (55%) were notified in the last two years (2011-2012). Genotype clustering rate was significantly higher in patients aged < 40 years (AOR 2.03) and the homeless (AOR 2.12), and lower for the foreign-born (AOR 0.21). Among a total 1018 patients, we found 32 patients who treated more than two times during the study period, of those, 12 were confirmed as reinfection cases indicating different genotype to their first episode of TB.

Conclusion: long term accumulated molecular epidemiological information indicated association of socio-demographic factors with genotype clustering.

Table Associations of factors with genotype clustering

Socio-demographic factors with genotype clustering	Adjusted odds ratio	95%CI lower	95%CI upper	P value
Age < 40 years	2.03	1.47	2.80	<0.000
Homeless	2.12	1.54	2.93	<0.000
Foreign born	0.21	0.12	0.36	<0.000
Male	1.25	0.90	1.72	0.180

PD-724-27 Strain diversity in *Mycobacterium tuberculosis* complex isolates between 2006 and 2015 in Bamako, Mali

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Background: Strain typing is a useful technique for understanding strain distribution and the dynamic of the disease spatiotemporal evolution. We used spoligotyping to identify the different strains of *Mycobacterium tuberculosis* complex (MTBc) circulating in Bamako between 2006 and 2015.

Methods: Between March 2006 and December 2015, we enrolled tuberculosis (TB) patients at the University Teaching Hospital of Point-G and three health centers in Bamako region and collected samples which were processed at the SEREFO BSL-3 laboratory under IRB approved research protocols. The diagnosis of tuberculosis was confirmed by the combination of fluorescence microscopy and culture of mycobacteria. MTBc cases

were identified based on colonial morphology and confirmed with nucleic acid probes (GenProbe®, Accuprobe) or Neo-Tauns Capilia® TB test, and spoligotyping was used to identify the circulating species and sub-species.

Results: During the study period, 1,330 cultures from 665 patients were performed. Out of the 665 patients, 314 (47.2%) isolates were typed. Three members of MTBc were identified: *M. tuberculosis* 253 (80.6%), *M. africanum* 58 (18.5%) and *M. bovis* 3 (0.9%). Overall, we found 15 different families. The three most predominant were: *M. tuberculosis* T family, 102 (32.5%); *M. tuberculosis* LAM family, 70 (22.3%); and *M. africanum* type 2, 54 (16.2%). Furthermore we found that *M. tuberculosis* T family was the most represented in treatment failure groups 58 out of 95 (61.1%), whereas *M. tuberculosis* LAM family was the highest in naïve tuberculosis patients 63 out of 210 (30%). It was also noted that while the prevalence of *M. africanum* was constant from 2006 to 2010 in the population at around 25%, it decreased from 2011 to 2015 to approximatively 15.1%, and this was associated with the occurrence of ancestral lineages of *M. tuberculosis* such as Haarlem and East African Indian (EAI) families.

Conclusions: Strain typing of MTBc isolates from tuberculosis patients in Bamako revealed 15 families, and showed a trend of strain evolution during the study period. Will *M. africanum* which is largely confined to West Africa is dying out from this population? Closed surveillance of this trend will allow a better determination of the true diversity profile of this region.

PD-725-27 Molecular epidemiology of *Mycobacterium tuberculosis* and its historical trends in South Korea, 1994-2006

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Background: Molecular epidemiology is a tool to discriminate recent transmission and reactivation of active tuberculosis (TB). The molecular epidemiologic information would be useful evidence to design and program national TB policy. In particular, rate of recent transmission would reflect the achievement of national TB policy. The study aims to identify clustering rate of active TB and its historical differences between the 1990s and 2000s in South Korea.

Methods: TB isolates were selected by sampling with probabilities proportional to size from Korean Mycobacterium Resource Centers (KMRC) stored in 1994-2006. IS6110 Restriction Fragment Length Polymorphism (RFLP) and 4-locus standardized mycobacterial interspersed repetitive unit-variable number tandem repeat typing (MIRU-VNTR) were used to identify clustering of active TB. Clustering was an outcome variable measured by three ways: RFLP only, MIRU-VNTR only, and both methods. Other covariates were measured, which include age, gender, region, and drug-

susceptibility testing profile. Uni- and multivariate analysis was conducted by STATA 13.0.

Results: Among 11 135 isolates stored in KMRC, 1151 isolates were selected for the study. After excluding contaminated isolates or cases without demographic information, 1,007 cases were analyzed. Clustering rates were at 19.7%, 35.8% and 4.7% in IS6110 RFLP only, MIRU-VNTR only and both methods, respectively. In multivariate analysis, younger age group (< 29) is more likely to be clustered than older age group (>49) in three different methods. In addition, the clustering rates were decreased in the 2000s compared to the isolates collected in the 1990s.

Conclusion: Trends of recent transmission would be higher chances in younger age group. On the other hands, older age group might be likely to be active disease by reactivation from previous latent TB infection. In addition, probability of recent transmission would be decreased in the 2000s compared with the 1990s, which may reflect partial success of national TB policy since the 2000s in South Korea. Therefore, future policy should be focused on the separated strategy by age groups to prevent direct transmission for young age group and reactivation for old age group.

PD-726-27 Genotypic and spatial analysis of multidrug-resistant tuberculosis transmission in a large metropolitan city in China

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Background: Multi-drug resistant tuberculosis (MDR-TB) has imposed serious risks on public health globally. China has the second largest number of MDR-TB patients globally, and a prevalence rate two times of the world average. The study aims to investigate the association of recent transmissions and spatial aggregation of MDR-TB patients in Shanghai, a large metropolitan city with a quarter of population being internal migrants.

Methods: We conducted a population-based molecular and spatial epidemiological study of all MDR-TB patients who were diagnosed and registered in Shanghai between 1 January 2008 and 31 December 2012. We defined genotype clusters as cases with identical variable number tandem repeats (VNTR) genotype patterns. Relative transmission rates were estimated by the index case's smear status, residential status and residential address. The spatial analysis included kernel density estimation (KDE), D-function analysis, a t-test distance analysis, and local K-function analysis.

Results: Among 367 MDR-TB patients, 318 (87%) MDR-TB patients had residential address and genotyped isolates, of which 135 (42.4%) were recent transmissions in 50 clusters. The relative recent transmission rates were 0.79 (95%CI 0.40-1.55) for smear negative patients

compared with smear positive patients, and 2.10 (95%CI 1.28-3.46) for local patients compared with migrant patients. MDR-TB patients were spatially concentrated in central urban area. Kernel density maps and the D-function analysis showed patients in the same genotyping clusters tended to be more spatially correlated, while the mean distance of genotypically clustered patients was significantly shorter compared with those not genotypically clustered (12.9 km vs 26.1 km; $P < 0.001$). Multivariate analysis indicated that the value of local K-function at 5 kilometers was the strongest factor associated with genotypic clustering (aOR, 7.22; 95%CI 2.05-26.73), however, the K-function became non-significant when using a K-function over 5 kilometers.

Conclusions: Recent transmission of MDR-TB was prevalent in Shanghai China. The significant association between spatial aggregation and genotypic clustering of MDR-TB patients revealed recent transmission of MDR-TB caused by a small subset of strains in relatively small neighborhoods within 5 kilometers.

PD-727-27 Discriminatory power of MIRU-VNTR for differentiating *Mycobacterium tuberculosis*

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Background: The transmission dynamics of *Mycobacterium tuberculosis* using markers has been studied globally and a particular marker for genotyping *M. tuberculosis* is the mycobacterial interspersed repetitive units (MIRU), which occur in variable number tandem repeats (VNTR) consisting of multiple loci. Tuberculosis (TB) remains an important public health problem in Sri Lanka and being a country of tourist destination and due to major development projects undergoing, it has a high proportion of tourists and immigrants from Asia and Europe that are characterized with highest TB incidences and drug resistant clinical isolates. Despite such a context, only a few investigations have addressed the question of *M. tuberculosis* genetic diversity and in this study, we investigated the discriminatory power of MIRU-VNTR typing of 15 and 24 loci to differentiate *M. tuberculosis* isolates.

Method: Acid fast bacilli positive sputum samples ($n = 150$) from first visit patients were collected from January 2012 to April 2014 from Central Province, Sri Lanka, and the ethical clearance was obtained from the Faculty of Medicine, University of Peradeniya. Decontamination of sputum was done using the modified Petroff's method and Lowenstein-Jensen medium were inoculated with the suspension. Genomic DNA was extracted from culture positives, strains of H₃₇Rv and *M. bovis* using standard CTAB/NaCl method. The isolates were characterized by two genotyping methods, spoligotyping and MIRU-VNTR for both the 15 and 24 loci.

Results: Both 15 and 24 loci yielded the same strains of *M. tuberculosis* except one strain of LAM, which is a T1 origin. 15 MIRU-VNTR yielded 57 clustered cases in 19 distinct clusters and 24 loci yielded 33 clustered cases in 14 clusters. 15 loci strain grouping had more clusters of strains grouped together while 24 loci differentiated the strains into distinct strain types.

Conclusion: 15-locus MIRU-VNTR typing is sufficient for a first-line epidemiological study to genotype *M. tuberculosis* but 24 loci MIRU-VNTR has been able to differentiate samples within highly homologous groups.

Table Discriminatory index and clustering rate

MIRU-VNTR locus set	Number of unique genotypes	HGDI	Clustering rate (%)
15 loci + spoligotyping	19	0.896	25.33
24 loci + spoligotyping	20	0.897	12.66
Spoligotyping	16	0.814	52.66

13. Spectrum of TB care in key affected populations

PD-728-27 When students become patients: TB disease among medical undergraduates in Cape Town, South Africa

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Background: Medical students in TB-endemic settings are at increased risk of latent TB. In South Africa, incidence of Tuberculin Skin Test conversion in medical students is 23/100 per year (95%CI 12-43). The burden and impact of TB disease in this population is unknown. **Methods:** Medical students and recent medical graduates who developed TB disease during their undergraduate studies (2010-2015) were eligible to complete a self-administered online questionnaire. The survey was digitally distributed to 3500 students, with 12 students self-reporting a diagnosis of TB disease during undergraduate training. Four students were selected for semi-structured interviews which were coded and analysed using the framework approach. Ethical clearance and institutional permission were obtained from the universities (Ref: S15/02/025; 331/2015).

Results: The disease spectrum of the twelve students (ten female) included pulmonary TB (6), pleural TB (3), TB lymphadenitis (2) and TB spine (1). Two students had drug-resistant (DR-TB) disease. Mean diagnostic delay post-consultation was 11 weeks, with only 42% of initial diagnoses being correct. Most utilized private healthcare providers (general practitioners [7]; pulmonologists [4]) and nine underwent invasive procedures (bronchoscopy, pleural fluid aspiration and tissue biopsy). Substantial healthcare costs were incurred (up to R25 000 for drug-

sensitive TB, R104 000 for DR-TB); few students had comprehensive medical aid cover. TB treatment was mostly obtained from government clinics, incurring large transport costs and missed academic time. Students with DR-TB interrupted their studies and experienced severe side effects (hepatotoxicity, depression and permanent ototoxicity). Most participants cited poor TB infection control (TB-IC) at the training hospitals as major risk factor for occupational TB. Although the experience of TB disease increased students' empathy with patients, they reported feeling greater vulnerability in the clinical environment. Students were stigmatized by colleagues and health care providers but found support from other TB survivors invaluable.

Conclusions: Undergraduate medical students in Cape Town are at high risk of occupationally-acquired TB disease. Comprehensive institutional support for students who develop TB disease is urgently needed, including free screening, diagnostic services and treatment. Healthcare workers should be recognized as key affected TB population, with resources invested in ending nosocomial TB transmission.

PD-729-27 Profile of health workers with TB in Brazil in 2015

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Background: The transmission of tuberculosis (TB) nosocomial can be considered an public health problem. In Brazil, there are many work settings where health professionals are inserted and directly exposed to the bacillo TB. The aim of this study is to describe the profile of health professionals in the treatment of tuberculosis.

Methods: This is a descriptive study of health profile professionals in tuberculosis treatment in Brazil, 2015. The cases of TB are reported and monitored by the National Notification System (SINAN). The following variables were analyzed: sociodemographic profile (gender, age, race, education), clinical form, culture and sensitivity test (exams performed) and associated comorbidities.

Results: In the year 2015 were registered in SINAN 645 new cases of TB in health care workers (82.3% of total cases), of these 57% were female, 31% were between 25 and 34 years old, 40% were no black and 26% had completed 11 years of estudy. The pulmonary form was 74% and the realization of culture 38%, the performed sensitivity test was not reported in 80% of cases. As for comorbidities: 9% were the result of positive testing for HIV, 10% reported being users of illicit drugs, 10% consumed alcohol and 12% smokers.

Conclusions: While recommending universal culture for health professionals largely does not have access to the exam, and the occupational risk for these professionals should be prioritized. It is also important to note the high proportion of illicit drug use, alcohol consumption and smoking in this group, highlighting the importance of support from the mental and psychosocial health

monitoring of these patients. The development of infection control plans is critical to initiate changes in the daily routine of health services at all levels of complexity, thereby reducing the risk of nosocomial transmission of tuberculosis.

PD-730-27 Health care worker screening at selected health care facilities in Namibia

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Background and challenges to implementation: In 2013 Namibia notified 10 610 cases of all forms of tuberculosis (TB). With a catchment population of 245 446 (2011) Ohangwena region situation in the northern part of the country accounted for 10% of the nationally notified cases (410/100 000), and 15% of the country's Drug Resistant (DR) TB cases. The burden of TB disease among health care workers is unknown despite the high disease prevalence in the region. The region chose to act. **Intervention or response:** Sensitization meetings were held with nurse managers and all Health Care Workers (HCWs), and symptom screening was done for all HCWs (747) with a standardized questionnaire. Symptomatic staff submitted sputum samples, which were tested using Gene Xpert.

Results and lessons learnt: Out of 754 HCW screened, 316 (42%) had at least one symptom of TB. Out of these 291 (92%) submitted sputum for further laboratory investigation. *Mycobacterium tuberculosis* was detected in 20(7%) of the samples, none of these had Rifampicin resistance. Nurses constituted 8 of the confirmed cases.

Conclusions and key recommendations: There is high TB incidence among health workers in Ohangwena region, possibly due to occupational exposure. There is however need for further studies to evaluate the role of occupational exposure in the development of TB among health workers in this setting. In addition routine TB screening for health care workers needs strengthening.

PD-731-27 Screening for TB in 600 000 Bangladesh garments workers

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Background and challenges to implementation: The garment workers of Bangladesh are usually migrant and impoverished and thus vulnerable to tuberculosis (TB). Prevalence has not been documented on a large scale, nor has there been a large screening programme for them.

Intervention or response: With two years of TB Reach funding spent over three years (April 2013 to March 2016) the Centre for Woman and Child Health (CWCH) in Savar/Ashulia screened 618 440 garment workers in

about 500 factories. The screening was rapid and covered all workers in factories. The screening team walked down production lines asking each worker 11 questions, which took about one minute. Suspects were referred to a team doctor who ordered chest X-ray (in a mobile X-ray bus) and collection of two samples of sputum for LED microscopy back at the CWCH path lab.

Results and lessons learnt: Of the 618 440 workers screened 17 640 (2.8%) were referred as suspects to the team doctor, who ordered a total of 823 all cases of TB were detected in the three years of screening: 427 New SS+, 242 New SS-, 245 New EPTB and 63 other forms of TB. This means the rate of TB in this population was 133 per 100 000. This active screening rate compares with Bangladesh NTP detection of about 110 per 100 000 through passive case finding in the general population. This rapid screening intervention has led to increased awareness about TB among garment workers, such that in the second half of the programme self referrals from garments workers, who were asymptomatic during screening, increased dramatically to 75% of all detected cases.

Conclusions and key recommendations: This programme cost about US\$1 per worker screened but the fund constrained NTP is yet to commit to continued screening. We are planning therefore to explore the possibility of incorporating TB screening in regular occupational health activities with active participation of buyers, owners, the NTP and the ILO.

PD-732-27 TB surveillance in Nunavut, Canada

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Background and challenges to implementation: Nunavut has some of the highest rates of TB in Canada, with annual age-standardized rates of disease ranging 25 to 45 times higher than in the rest of Canada. In 2014, there were 277.17 active cases identified per 100 000. Nunavut is Canada's most northern and isolated territory, comprised of 22 small communities accessible only by plane. The population is predominantly Inuit, a group that has faced many challenges resulting from ongoing colonialization and the government's historical approach to TB control. Health service delivery is often difficult due to high turnover, lack of staff, and limited resources in remote communities. While expansion of communications networks is planned, current infrastructure does not support electronic health information systems in all communities.

Intervention or response: In the absence of a comprehensive public health information system, the department of health designed and created its own interim solution for collecting and housing TB data for active cases, latent infections, and for surveillance of high-risk individuals. The system was designed to be user-friendly for nursing staff users and streamlined enough to allow data to be exported and emailed to territorial staff given the current challenges in telecommunications. Data

elements were chosen carefully to balance feasibility with the need to collect as much quality data as possible.

Results and lessons learnt: After an iterative trialing process in collaboration with the regional staff responsible for using the system, the database was rolled out throughout the territory. Regional communicable disease coordinator nurses were responsible for entering data from paper forms submitted by front-line staff. Data was retroactively entered for all of 2015 and compiled and analysed for annual surveillance and reporting at the territorial level. The model was so well-received by staff that it is being replicated for syphilis surveillance. The combination of case management and surveillance needs met by the system made it particularly useful for both regional and territorial staff.

Conclusions and key recommendations: A simple home grown TB information system can reduce the reporting workload for TB surveillance, and can provide a bridging tool in the transition from paper to electronic surveillance.

PD-733-27 Optimizing quality in tuberculosis control in Northwestern Ontario

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Background and challenges to implementation: First Nations people continue to be disproportionately affected by tuberculosis (TB) disease at a rate of 21.8 per 100 000 people in Canada, nearly five times the national average. The continued presence of tuberculosis disease in Northwestern Ontario demonstrates public health challenges on-reserve. Previous reports highlight public health deficits on-reserve and unclear trans-jurisdictional roles between federal, provincial, and First Nations governments.

Intervention or response: Using qualitative research methods, this study set out to define the cascade of care for patients with tuberculosis disease in Northwestern Ontario, including diagnosis, active management, follow-up, and contact tracing. Observations were conducted on-site in Sioux Lookout, Ontario. Semi-structured interviews with 12 stakeholders from different levels of health care delivery were recorded, transcribed, and qualitatively analyzed. Agency policy guidelines were compared with national and international TB guidelines. Patient cases were reviewed to assess the interaction of real individuals with the cascade of care.

Results and lessons learnt: The cascade of care for persons with suspected tuberculosis disease living on-reserve in Northwestern Ontario was defined and analyzed through the patient perspective. Through interviews and on-site observation, barriers to the effective delivery of TB care on-reserve were identified, including lack of provider knowledge of disease, guideline applicability, and available supports; diffuse fiduciary political responsibility; outdated and disjointed communication of health information; and lack of public

health infrastructure and resources on-reserve. Analysis of local, national, and international TB guidelines yielded recommendations for improving the delivery of public health in Northwestern Ontario.

Conclusions and key recommendations: Clarification of jurisdictional roles and responsibilities has the potential to improve the effectiveness of various stakeholders in TB control and may result in the reduction of drug-resistance in Canada. Further development of public health infrastructure on-reserve, educational programs for primary care providers, and improved communication between providers are tangible goals that can improve the delivery of public health and TB disease identification and management on-reserve. Leadership is needed to address gaps in communication between providers and the trans-jurisdictional issues involved in health care delivery to First Nations peoples.

PD-734-27 Sustained community intensive initiatives saved lives of primitive tribe communities in Kawardha district, Chhattisgarh, India

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Background and challenges to implementation: TB remains a major public health problem amongst the tribal population. One-third of the Chhattisgarh populace is home to 42 tribes, most of which are Primitive Tribal Groups (PTGs), of whom ≥ 40 with *Baiga* PTGs are concentrated in 2 blocks in Kawardha district. Their health status is extremely poor due to long lasting malnutrition, lack of proper hygiene, illiteracy and archetypal traditional health seeking behaviour. Poor physical access to diagnosis and treatment under RNTCP and public health services not being community friendly in terms of timing, cultural barriers inhibiting utilization are a few key hindrances to address for these PTGs. Mortality due to TB is the highest among these ancient communities, reported with *One Death per Minute*.

Intervention or response: Community intensive activities like guided community & peer meetings, patient-provider interaction, out-reach events, pictorial display & community radio program aired on TB and health awareness campaigns were conducted by the program in the two *Baiga* tribe dominated blocks during 2015. 32 community volunteers including 12 cured TB persons of the *Baiga* community were trained and engaged who reached out to the villages by visiting on door-to-door basis and informed about TB, its symptoms, diagnosis, treatment, and RNTCP services and counselled them to avail these services by referring, collecting/transporting sputum to the Designated Microscopic Centres and linked to DOTS upon diagnosed as TB. During treatment, all 67 patients were ensured with nutritional food supplementation from the Public Distribution System facility.

Results and lessons learnt: 75 villages, 12 500 households with 58 000 *Baiga* population were reached. 67 positive TB patients diagnosed and put on DOTS from sputum examination of 482 presumptive TB cases referred/sputum collected and transported through community volunteers during the period. 28 patients were cured while 39 are under treatment. Saved 67 lives. 6 cured persons and 12 *Baiga* community girls were trained as DOT Providers.

Conclusions and key recommendations: Reaching out with tuberculosis services among the socio-culturally isolated ethnic groups on a sustained approach by engaging the community themselves and by adapting out of box strategies will bring a significant impact on the disease prevalence and mortality in the community.

Figure Intervention area



PD-735-27 To achieve WHO Post-2015 Targets: simplified scoping review for TB epidemiology and programmatic response in the elderly in Hong Kong

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Background: Ageing in the population is increasingly becoming a global challenge of TB control especially in the developed world. In Hong Kong, a developed city with intermediate TB burden, it was found as the main reason for TB stagnant endemic after 1990s. In order to achieve WHO End TB target, we conducted a scoping review to identify the epidemiology of and programmatic response to TB in elderly in Hong Kong, to explore research gaps and insights for policy improvement.

Methods: The scoping review was conducted through government reports, technical guidelines and literatures. Articles written in English and published before 31 December 2015 were reviewed in major electronic databases, with key words of 'tuberculosis', 'aged' ('elderly' or 'old people'), and 'Hong Kong'. Based on specific inclusion criteria, we investigated TB infection, incidence, case finding, treatment and outcome, risk factors, control strategy, health system and services.

Results: In Hong Kong, elderly was found as an important aspect in TB annual reports and TB manual. A total of 33 articles were included for review analysis. The proportion of elderly among patients was increasing from 15.3% in 1985 to 39.0% in 2004 and then level off. In 2013, they accounted for 75% of all TB deaths. High TB infection rate (43.8%, 68.6% and 46.3%) was found in elderly and they were more likely to develop TB by endogenous reactivation. Their prevalence and notification rate remained high with little change and increased with age. The elderly patients were more likely to be male, current and ex-smokers, weighing less (BMI < 18.5 kg/m²), having seasonal frequency and geographic distribution, a past history of TB and coexisting medical diseases, longer delay in presentation and commencement of treatment, low drug resistance, adverse effects and unfavorable treatment outcome.

Conclusions: This review demonstrated a high TB burden and specific characteristics in elderly patients in Hong Kong. However, few studies were found in terms of control strategy, health services and care, patient awareness and behavior, treatment adherence and qualitative investigation. Further research is needed to explore and the programmatic response and strategy improvement.

PD-736-27 Risk factors for developing tuberculosis among the national HIV-positive cohort over 15 years in England, Wales and Northern Ireland

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Background: Tuberculosis (TB) is a common co-infection of people living with HIV (PLHIV), leading to poorer clinical outcomes and increased risk of death. We describe the epidemiological profile of TB among PLHIV in the UK and risk factors for developing TB after HIV diagnosis.

Methods: Adults aged ≥ 15 years diagnosed with HIV and TB were identified by linking national HIV and TB surveillance datasets. PLHIV first presenting to health services in England, Wales or Northern Ireland between 2000-2014 were followed until TB diagnosis, death, or 31 December 2014, whichever was soonest. To investigate risk factors for developing TB, we calculated incidence rates of TB per 1000 years follow-up and estimated approximate hazard ratios (HRs) using univariable and multivariable Poisson regression models. CD4 count was included as a time-updated covariate.

Results: 95 003 adults were included; 42.1% were men-who-have-sex-with-men (MSM), 54.8% were heterosexual and 2.2% were people who inject drugs (PWID). 46.0% had white ethnicity and 37.8% black African. At HIV diagnosis, median age was 34 years and median CD4 count was 340 cells/ μ l. Median follow-up period was 7.3 years (range 0.3–15.0). There were 2187 TB cases during 652 842 person-years (PY) follow-up. Overall TB incidence post-HIV diagnosis in PLHIV was 335 cases/100 000 PY; 854 in male PWID, 592 in female PWID, 560 in heterosexuals and 108 in MSM. Incidence was 105 in white, UK-born individuals, 350 in black African UK-born individuals and 629 in black Africans born in high TB-incidence countries (>40 cases/100 000). In multivariable analysis, TB risk increased with decreasing CD4 count; compared to CD4 ≥ 500 cells/ μ l, the HR increased from 1.71 (1.44–2.03) for CD4 350–499 to 19.86 (16.43–24.01) for CD4 0–49. TB risk was greater for UK-born black Africans (HR 2.44 [1.60–3.23]) and individuals born in high TB-incidence countries (white ethnicity: 2.39 [1.74–3.30]; black African: 4.55 (3.74–5.55); other: 3.80 (3.01–4.80)) compared to white UK-born individuals. TB risk was higher for heterosexuals (1.49 [1.25–1.78]) and PWID (male: 4.49 [3.43–5.89]; female: 3.99 [2.50–6.38]) than MSM.

Conclusions: Greater focus on screening and care interventions for PWID, black Africans, individuals born in high TB-incidence countries and those with low CD4 count may decrease TB incidence in PLHIV.

PD-737-27 Tuberculosis and pregnancy in a cohort of women receiving antiretroviral therapy in Ethiopia

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Background: The introduction of antiretroviral therapy (ART) has transformed the lives of many women living with HIV, and has reduced suffering from co-morbidities and co-infections such as tuberculosis (TB). With improvements in quality of life, most women desire to have children, especially in settings where having a child is viewed as a valuable asset. However, there is limited information on the frequency of pregnancy and appropriate family planning approaches in these settings. Integrating family planning interventions with efforts to prevent and control TB could serve as viable entry point. As an exploratory step to generate evidence, we analyzed information on the magnitude of both TB and pregnancy in a cohort of women receiving ART.

Methods: This was a retrospective cohort study carried out in six hospitals in two regions of Ethiopia, as part of a long-term treatment outcome study. We analyzed the rates of reported pregnancy and TB among women of reproductive age, and calculated incidence rates as the number of events per 100 person-years (PY) per younger and older age groups. We used Cox Regression analysis for adjusted analysis.

Results: Among 773 women age 15–44, 81 pregnancies were reported during 2899 PYs (2.8 per 100 person-years). In women aged 15–24, incidence rate was 48/972 (4.9 per 100 PY) compared with 33/1926 (1.7 per 100 PY) in 25–44 yr olds. Unadjusted hazard ratio (HR) for pregnancy was significantly higher among younger age groups: unadjusted HR (95%CI) = 3.15 (2.01–4.92; $P < 0.0001$). After adjusting for marital status, pregnancy rate remained higher for the younger age: HR (95%CI) = 3.49 (2.43–6.50). TB incidence rate was also higher in the younger age group (2.8 per 100 PY) compared with the older age group (1.3 per 100 PY). After adjusting for CD4 count, the HR for TB in the younger age vs. older age remained significant: HR (95%CI) = 2.04 (1.16–3.59; $P = 0.013$).

Conclusions: Young women receiving ART are at increased risk of TB, and are more likely to become pregnant. The existing collaborative TB-HIV platform can be used to address the reproductive and family planning needs of women of reproductive age.

PD-738-27 Integrating TB screening in routine antenatal care services through engagement of lay providers: lessons from Kampala

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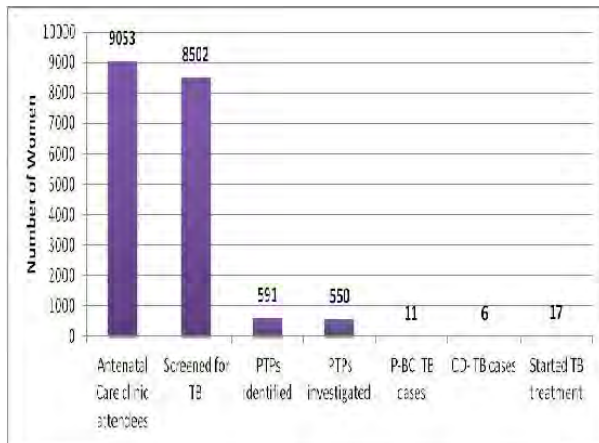
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Background: In Uganda, antenatal care providers are oriented and provided with a register to document TB screening results, but only about 10% of mothers who attended ANC at Mulago Hospital were screened for TB. The prevalence of active TB in this setting is not known. We piloted systematic screening of pregnant women who attended ANC at Mulago to determine the prevalence of active TB in this population.

Intervention: Mulago ANC team with support from USAID-funded Track-TB project organized routine TB screening for ANC attendees through engagement of a community volunteer seconded by AIC between October and December 2015. The volunteer administered standard screening questions of the intensified case finding form, separated symptomatic mothers, and linked them to the clinician for further clinical and laboratory evaluation using GeneXpert. Diagnosed TB patients were initiated onto TB treatment. Biweekly, the team reviewed TB screening data, performance and processes. **Results:** 94% of 9053 mothers who attended ANC between October and December 2015 (Figure) were screened, up from 10% before the intervention; 591 PTPs (6.95%) were identified and 550 (93.1%) evaluated in the laboratory; 17 TB mothers were diagnosed with TB and started on treatment. This is almost equivalent to the estimated prevalence in the general population and it is much higher than previously estimated among pregnant women (2.3/1000). Integrating TB screening in high volume antenatal clinics is feasible and can be effectively executed through task shifting to lay providers.

Conclusion: The prevalence of TB among women attending routine antenatal care services is much higher than previously estimated. We recommend further research and involvement of lay providers to strengthen TB screening and evaluation in ANC care setting to increase TB case finding, treatment and control.

Figure TB screening cascade in an antenatal care setting. (Data source: Antenatal care, presumptive TB, Laboratory and TB treatment registers.)



14. Implementing tobacco control strategies

PD-739-27 City made free from tobacco product hoardings and boards without litigation through self removal and signed declarations by shopkeepers

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Background and challenges to implementation: GYTS 2009 says 74.4% adolescent and youths saw pro cigarette ads on bill boards, GATS quotes 34.5% adults noticed cigarettes, 58% Bidi and 63.3% smokeless tobacco advertisements. Under section 5 of Indian Tobacco Act - COTPA 2003, advertisements are prohibited and violation is non compoundable. Enforcers did not want to appear personally in court frequently for too many cases; however court expects the officers even he is transferred to other place. Unfortunately, tobacco companies use big display boards and posters to advertise their products. Enforcers were not trained and skilled to handle this problem.

Intervention or response: 1) The District Collector-cum-Chairperson, Tobacco Control Committee informed about violation through evidence, photographs and numbers of boards available in the city. 2) Collector issued directives, one week warning announcement made in the city. 3) Some of the shopkeepers and advertisers removed their hoardings but the majority remained the same. 4) Monitoring-cum-enforcement team formed involving 3 departments, i.e., Corporation, Police and Administration. Training organized and monitoring started. 5) Shopkeepers were given the option either to remove and destroy the hoardings/ bill boards by

themselves and give signed consent not to violate the section 5 in future or go for litigation.

Results and lessons learnt: Most of the tobacco shopkeepers opted not to go for litigation. Of 100 hoardings / boards, 800 were removed and destroyed by the shopkeepers themselves. Around 750 shopkeepers gave written declaration that they will never display hoardings/boards in future. City has been made almost free from tobacco advertisement boards and hoardings. Municipal Corporation decided to remove all illegal boards in their routine checking. Awareness, monitoring and enforcement should go together. Strict implementation with innovation reduces stress of the implementers. Officers do not have to appear in the court. Written declaration is an indirect pressure on shopkeepers and helpful in sustaining the process.

Conclusions and key recommendations: Systematic, strict implementation clubbed with innovation reduces the pressure of implementers and is helpful in bringing the desired results.

PD-740-27 Comparison of tobacco control programs worldwide: a quantitative analysis of the 2015 MPOWER report

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Background: The World Health Organization (WHO) introduced a package to parties including six main policies to control tobacco use on 2008. A report of the activities of countries worldwide is published once every two years by the WHO. Our objective was to perform a quantitative analysis of MPOWER in countries and regions to make challenges between parties.

Methods: This cross-sectional study collected information using pages 118 to 129 of the 2015 MPOWER report by a validated check list. For assessment of the 10 criteria included in the report of each country, a 0–4 point scale was used for scoring the five-item and a 0–3 point scale was used for scoring of the four-item criteria. Maximum score was 37. The scores were entered independently by two individuals and a third party compared the values and confirmed their accuracy. The scores were summed and presented in a descending order.

Results: Fifteen countries, which acquired the highest scores (85% of total 37) included Panama and Turkey with 35, Brazil and Uruguay with 34, Ireland, UK, Iran, Brunei, Argentina and Costa Rica with 33 and Australia, Nepal, Thailand, Canada and Mauritius with 32 points.

Conclusion: Countries perform differently with regard to tobacco control programs and each country must work on its weaknesses and reinforce its strengths. Comparison of scores of different countries in this respect can be beneficial since it creates a challenge for the countries to achieve a higher rank.

PD-741-27 Prevalence of tobacco use among priests and their willingness to spread anti-tobacco messages among devotees in Delhi

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Background: Tobacco use has increased in India in recent times. Hence, need for intensification of tobacco control efforts become pertinent. Tobacco cessation involves behavior change and evidence suggests that religious professionals may be helpful in community based smoking cessation programs. Therefore, the current study was done to assess the prevalence, knowledge and practices related to tobacco use among priests and their willingness to spread anti-tobacco messages among their devotees.

Methods: It was a community based, cross-sectional study conducted amongst 159 head priests of Delhi. A semi-structured interviewer based questionnaire containing items to assess socio-demographic characteristics, tobacco use behavior, their knowledge about harmful effects of tobacco and willingness to spread anti-tobacco messages among devotees, was used for data collection.

Results: Out of the total 159 participants, 86.2% ($n = 137$) were males. There were 61% ($n = 97$) Hindus followed by 18.2% Muslims ($n = 29$). Thirty seven respondents (23.3%) reported to be the current users of tobacco. Among the current tobacco users, 32 (86.5%) were using more than one form of tobacco. The most common form of tobacco being used was 'chillum' pipes ($n = 31$; 83.8%). The knowledge about harmful effects of tobacco use was less among tobacco users as compared to that of non-tobacco users. However, majority of them ($n = 152$; 95.6%) expressed their willingness to spread anti-tobacco messages to their devotees irrespective of their smoking status and also desired to be trained in the same.

Conclusions: The prevalence of tobacco use was low among the priests. Majority of them expressed their willingness to spread anti-tobacco messages. Therefore, religious leaders should be motivated through training in tobacco use prevention and helped in implementing tobacco use cessation activities.

PD-742-27 How West Bengal has been enforcing smoke-free policies. An assessment from India

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Background: Smoking in public places is prohibited under Cigarette and Other Tobacco Products Act (COTPA) 2003. However, GATS (2010) data revealed that in West Bengal 21% people are smokers and 42% adults are exposed to tobacco smoke in their workplaces and almost 30% people exposed to SHS in public places. Present study was conducted with the objective of

assessing and ascertaining the present status of smokefree policies in selected districts of West Bengal, India.

Methods: In each of the 5 purposively selected districts of West Bengal a minimum of 30% of the clusters (Municipalities/Corporation and administrative Blocks) were selected randomly for collecting samples. The sample size has been enumerated at the level of 95% confidence interval with 50% compliance rate while the design effect of the study was 1.0. The Epi-info 7 software has been used for the purpose. Smokefree compliance assessment was done using the 'Assessing compliance with smoke-free laws' guide jointly developed by Johns Hopkins, The Union and CTFK. After collection and tabulation of data it was further analyzed statistically with some associated tests like percentage analysis, compare mean, t -test to get the proper results.

Results: Overall, 83.7 % public places do not have any kind of 'No smoking' signage. Only 0.9 % public places, wherein signages as specified in the law, are there in place. Out of that only 0.2 % has mentioned designated reporting person's name. No active smoking was found in 76.3% of public places but there is evidence of smoking in 53.5 % public places. In T-test of two Municipal Corporations under study, it was found that Kolkata is significantly high up in active smoking (t -value 1.654), presence of smoking aids (t -value 6.544) and evidence of smoking in public places (t -value 8.817) in comparison with Howrah Municipal Corporation.

Conclusions: The results show that there is poor enforcement of smokefree policies in West Bengal. These are being shared with various stakeholders to prioritise SF enforcement in the state. However, these evidences will also be used to forcefully justify the need for effective enforcement of the law to its very letter and spirit.

PD-743-27 Compliance with smoke-free legislation among Istanbul hospitality premises in 2015

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Background: The data on compliance to smoke-free legislation in Turkey is limited.

The objective of this study was to determine violation rates and their change in years in enclosed spaces of hospitality establishments in Istanbul and also to evaluate the factors associated with non-compliance.

Methods: This study was designed as a cross-sectional survey and done using the same method of 2013 and 2014 studies. Four out of 39 districts in Istanbul were determined as the study area. Data were collected through direct observation. The observation form and the questionnaire were adapted from the guide on 'Assessing compliance with smoke-free law'. Observation were done at 12:00–15:00 and if smoking was not observed the establishment was revisited after 21:00.

Results: Of the 450 premises studied in 2013, 82% were found in 2014 and 71 % in 2015. The total rate of violations were found as 50.3%, 30.0 % and 24.4% in

2013, 2014 and 2015, respectively. Observation of tobacco use on site was found as; 35.3%, 25.9% and 21.0%; ash trays and substitutes 56.1%, 75.3% and 77.7% in three consecutive years. Non-compliance in bars were 84.6% in 2013, 76.9% in 2014 and 46.2% in 2015. Smoking outside hospitality premises were noted as; 25.3% in 2013, 31.3% in 2014 and 13.9% in 2015.

Conclusions: In spite of the decreasing trend in non-compliance in the sixth year of the legislation, one out of every four hospitality premises were observed to be violating the law.

PD-744-27 Legislating and implementing a smoke-free law by applying evidence-based data on smoking-attributed mortality, Tianjin, China, 2010–2014

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Background: To collect data and analyze smoking-attributed mortality in order to promote awareness of tobacco control as well as legislate and implement a smokefree law.

Methods: Adding information of smoke status in the death certificate, collecting and sorting data with All Cause of Death Surveillance System. The Relative Risk of smoking attributed mortality was analyzed by multilogistic regression. These evidence based data were interpreted into smoking harm and disseminated by diversity channels so that the policy makers and public support to legislate against smoking in public places according to FCTC in Tianjin.

Results: The total of 202 249 deaths aged 35–79 were registered during the study period. The three leading causes of death attributable to smoking were lung cancer, ischemic heart disease and cerebrovascular diseases for male and ischemic heart disease, lung cancer and COPD for female. The RR of male was 1.38 (1.33–1.43) with all cause of death and 3.07 (2.91–3.24) with lung cancer while the RR of female was 1.46 (1.39–1.54) with all cause of death and 4.07 (3.81–4.35) with lung cancer due to smoking, respectively. And for 35 years old men and women current smokers, they would individually lose 8 and 5 years of life on average attributed smoking. These evidenced based data were disseminated by mass media, official reports, news release, lectures, new media, and so on. Almost 40 000 citizens could read the related information and the support rate was up to 98% for banning smoking in public places. The Tianjin Smoke Free Law according to FCTC was issued and implemented on 31 May 2012. Before and after the law, public awareness about smoking causes lung cancer increased from 88.7% to 95.4%, heart disease increased from 58.0% to 75.0%, and stroke increased from 25.2% to 66.2%. The SHS was going down from 64.3% to 37.8%, the cases of heart attack in hospitals showed declining trend in indoor occupational population

($\beta = -0.0611$, $P = 0.0018$).

Conclusions: It is important to analyze and disseminate the evidenced based data of tobacco harm such as smoking attributed mortality that promoted to legislate and implement smoke free law in a large city with population over 10 million in China.

PD-745-27 Can the MPOWER tobacco control measures help countries achieve the 2025 tobacco control target?

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Background: In 2013, WHO Member States adopted a voluntary global target of a 30% relative reduction in prevalence of current tobacco use (smoking and smokeless) in persons aged 15+ years to be achieved by 2025 (using 2010 as baseline). To assist its Member States achieve this target, WHO supports the implementation of the WHO Framework Convention on Tobacco Control (WHO FCTC), and in particular its selected demand reduction measures which WHO badged under the acronym MPOWER. The paper aims to assess the impact of MPOWER on smoking prevalence rates.

Methods: Applying a Bayesian meta-regression using a negative binomial model to country tobacco survey data, WHO has been modelling trends in tobacco smoking for the period 2000–2012 with projections to 2025. In parallel, since 2008 WHO has been tracking the status of the MPOWER measures for all Member States in the series *WHO Report on the Global Tobacco Epidemic*, using a five-level categorization ranging from lowest to highest level of achievement. Countries with at least four MPOWER measures in place at the highest level in 2014 were grouped and their tobacco use prevalence trend compared with other countries that had only three or less MPOWER measures in place at the highest level of achievement.

Results: Substantial differences can be seen in tobacco use prevalence trends in countries with a high coverage of MPOWER measures at the highest level of achievement: Countries with at least four MPOWER measures in place at the highest level are more likely to achieve the tobacco use prevalence target than those countries with only three or less measures in place. This demonstrates that the MPOWER measures, if put in place at the highest level, are effective in helping countries to achieve their tobacco use target.

Conclusions: The results indicate that the MPOWER measures can help countries protect their populations from the harms of tobacco. Despite this success, significant gaps remain in establishing effective tobacco control measures in many countries and WHO is ready to support governments in effectively addressing the tobacco epidemic by incorporating all provisions of the WHO FCTC into national tobacco control legislation and programmes.

PD-746-27 Fifty per cent reduction in sales of tobacco products near educational institutions within 2 years in Himachal Pradesh, India: a comparative study

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Background and challenges: Himachal Pradesh a northern hilly state is a famous tourist destination in India. There are more than 40 000 thousands schools in Himachal Pradesh. The state has a high prevalence of tobacco use and sale of tobacco products was very common near the educational institutions irrespective of ban under the provisions of Indian Tobacco Control law (COTPA 2003). The baseline cross sectional study conducted in 2013 shows that tobacco is sold within 100 yards of 89% educational institutes. A massive campaign led by NGO HPVHA with health department in collaboration with the education department reduced the prevalence by 50% in two years time.

Intervention: A mapping of all such vendors was done in 2013. Notices through newspapers and directly to the vendors followed sensitization of the head of all educational institutes, parents, local bodies and local leaders in a phased manner. The top health authorities and top educational authorities issues circulars /directions to advise the people and panelize the violators under the law. The flying squads teams were mobilized to conduct periodic search operation to act against the violators. The Compliance study was repeated in 2015.

Results and lessons learnt: There has been a substantial progress in ban on sale of tobacco in the state in two years. The prevalence of such vendors declined from 89.03 % in 2013 to 45.88 % in 2015. It has been observed that most of the violations are in urban areas of the State.

Conclusion: Reducing sale of tobacco near educational institutes is one of the most effective demand reduction strategies for tobacco control. There is a need focused interventions and support from parents, teachers and local bodies.

PD-747-27 Investment and getting back the reward: training different government agencies to implement the tobacco control law in Bangladesh

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Background and challenges to implementation: Tobacco leads to chronic detrimental effects on health. To protect the public health, the Bangladesh government has directed all officers who have the magistracy power to conduct mobile court on different laws frequently at all levels. For last few years a mobile court drive was a very powerful tool to implement tobacco control law. So, it was an urgent obligation to sensitize the agencies on tobacco control law and are involved in implementation of law. The objective was to curb the tobacco epidemic through investment, i.e., to train them on tobacco control law for

building capacity and getting back the reward, i.e., to monitor the outcome following their training.

Intervention or response: The National Tobacco Control Cell has conducted training for the Executive Magistrates, Senior Health Education Officers, Sanitary Inspectors, Industry Inspectors, Police Officers, Ansar Officer, Civil Defense Officers and other authorized officers since 2012 in different batches throughout the year and trained 443 personnel of above mentioned law enforcing agencies. Then their initiatives were monitored through collecting report from concerned offices. It was a great challenge to ensure their participation from across the country, but made possible by the kind endeavor of the stakeholder Ministries.

Results and lessons learnt: Following the training, those officers conducted remarkable amount of mobile courts in different public places and public transports and made exemplary penalties. For instance, during January to September 2015, 816 mobile courts were conducted and penalized 2053 persons and 80 stores and companies and collected an amount of BD Taka 548 005 as fine for violating tobacco control law. It has received tremendous support from peoples from all walks of life and huge media coverage. Such action made people law abiding.

Conclusions and key recommendations: Such investment did not go in vain and found very fruitful. It gave an important message to the decision makers to continue more and more novel approaches for curbing the tobacco use.

PD-748-27 Cigarette pricing strategy in India: an example from Patna city, Bihar state

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Background: Bihar is home of about 53.5% (or 30.8 million) adult tobacco users. Out of this 14.2% (2.7 million) smoke, and expose nearly 25% of the rest of the adult population to second hand smoke (SHS) at public places and 60% at home. We surveyed the different types of cigarette brands and price (pack and singles) at which they are sold in different neighbourhoods of Patna city (pop: about 2 million).

Objective: To assess if there is a difference in brand dispersion and price variation in cigarettes based on class composition of neighbourhoods in the city.

Study methods: We collected data between March 2014 and March 2016 from 12 vendors in three types of habitations (rich, middle class and urban slums) of Patna city for one full day for each vendor. Ethical approval for conducting the survey and interviews was taking from the International Union Against Tuberculosis and Lung Disease Ethical Advisory Group (The Union EAG) in December 2013 (application 213/2013).

Results: Our findings suggest that cigarette pack and single prices vary with the composition of neighbourhoods where cigarettes are sold.

Conclusion: Brands are placed based on economic status of habitation, and even where the same brands exist price

variability of cigarette is nearly 20% for pack and about 40% for single sticks. Cigarette industry strategically segment positioning its brands. There is need for an in-depth study to understand if pricing varies based on other parameters (for example, is it cheaper around educational institutions).

15. Tobacco industry interference

PD-749-27 Monitoring the tobacco industry in Africa for effective implementation of the FCTC

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Background and challenges to implementation: The tobacco industry (TI) has been operating for many years in Africa with the deliberate purpose of subverting the efforts of the WHO to control tobacco use. In response to Article 5.3 of the WHO FCTC to protect public health policies from the commercial and other vested interests of the TI, the African Tobacco Control Alliance (ATCA) implemented, as from 2014, a project in 7 African countries to monitor, counter and expose the TI and support the adoption of FCTC-compliant policies.

Intervention or response: The project was carried out by ATCA's network of Civil Society Organizations (CSOs) in seven African countries. Each country set up a surveillance network of the TI, including civil society, governments, journalists and the WHO. Awareness was built on FCTC Article 5.3 among stakeholders, including parliamentarians. The capacity of CSOs and journalists to monitor, counter and expose the interference and tactics of the TI at national levels was strengthened. ATCA conducted intensive advocacy campaigns towards policy makers and influential groups and refuted claims of the tobacco industry regarding its economic contribution to the economy.

Results and lessons learnt: The project made policy-makers and influencers more aware of the systematic attempts of the tobacco industry to undermine tobacco control. In some of the target countries, parliamentarians openly discredited the tobacco industry and called for policy change. The media increased coverage on tobacco control issues. The project also generated greater synergy for tobacco control among different sectors, leading to increased public demand for tobacco control measures. All these factors contributed in the adoption of FCTC-compliant legislations in three of the target countries while the others initiated the process of drafting their TC bill.

Conclusions and key recommendations: The tobacco industry represents a major challenge to FCTC implementation in African countries. It has the power and resources to influence decision-making at the highest levels of government. The project indicates that multi-sectoral collaboration and common strategies are key in countering the tobacco industry. Sustained monitoring and discrediting of the industry contribute in destroying its public image and advance tobacco control.

PD-750-27 Protecting minors from tobacco use by prohibition of tobacco sales near an educational institution: an impact analysis from 10 districts

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Background: India's Cigarettes and Other Tobacco Products Act (COTPA) 2003 prohibits tobacco sales within 100 yards of educational institutions. Under section 6(b) of COTPA, educational institutions are required to display a mandatory signage outside the institution stating sale of tobacco product within 100 yards of this institution is a punishable offense with a fine up to Rs 200. A study was conducted to assess the compliance of section 6(b) near education institutions in 10 districts of Karnataka, India.

Methods: An observational study was conducted year 2013 in 10 public and private primary, secondary and college educational institutions as sample size across 10 districts of Karnataka, India where institutions and points of sale were assessed for its compliance to section 6(b) by use of a structured pre-tested checklist. A repeat study was conducted in 2015.

Results: In the year 2013, only 24% ($n = 1065$) had mandatory signage. 2% of vendors were selling tobacco products inside the campus and 40% ($n = 1411$) within 100 yards of the boundary. Whereas in 2015, 68.54% ($n = 2236$) of educational institutions displayed section 6(b) signage. Only 0.54% of the vendors sell tobacco products inside the campus. 12% were selling tobacco products within 100 yards of the institution's boundary.

Conclusions: Regular enforcement and advocacy efforts help in protecting minors from accessing tobacco products.

PD-751-27 Tobacco industry interference at point of sale in Argentina

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Background: Since 2011, Argentina has a national legislation that bans tobacco advertising and promotion in all media, except for points of sale (POS). At POS, however, advertising is allowed with certain limitations: it cannot be seen from the street and it only allows for up to two signs of 30 cm by 30 cm that includes a warning label covering at least 20% of the sign. Illuminated signs and 3D ads are also banned.

Objective: To assess the tobacco industry's (TI) compliance with the restrictions imposed at POS in three cities and the province of Buenos Aires, Argentina.

Methods: We analyzed 286 notices of infraction that the National Tobacco Control Program issued from December 2014 to December 2015 in the cities of Buenos Aires, Córdoba and Mendoza, and the province of Buenos

Aires. Notices included pictures of the POS that helped identify the number, size, and characteristics of the ads displayed at the POS. Visibility from the street was also noted.

Results: Of the 286 notices that were evaluated, 212 were from Buenos Aires, 13 from Mendoza, 13 from Cordoba and 35 from the province of Buenos Aires. Thirteen had to be void because they did not include the required information. One hundred per cent of the POS had signs that were above the permitted size. In almost 90% of cases, the signs were visible from the street. In 80% of cases, the POS exceeded the number of permitted signs and in 70% of cases the signs had lights that were on. The POS also displayed cigarette packs as an advertising medium.

Conclusions: The TI is using the POS to advertise their products and by doing so, violating the existing legislation. The existing legislation should be revised to implement a complete ban of advertising and promotion to limit the possibility that the TI uses the POS as a mean to overcome the regulation.

PD-753-27 Legal and metalegal strategies employed by local government to combat tobacco industry interference: Philippines best practices and practical lessons

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Background and challenges to implementation: The tobacco industry has scaled up efforts to prevent Philippine local governments from fully implementing strong and effective tobacco control policies in line with the WHO FCTC. Local government units (LGUs), whether at the regional, provincial, city, municipal or barangay level, have been successfully used legal and metalegal strategies in combating the challenges brought about by an active tobacco industry lobby. This research compiles a list of best practices and practical lessons in implementing Article 5.3 of the WHO FCTC initiated by selected LGUs in the Philippines; specifically: Iloilo City, Balanga City, Municipality of Daraga, Province of Capiz, and Province of Misamis Occidental.

Intervention or response: LGUs across the Philippines have implemented community-based initiatives to combat tobacco industry interference and continue to make use of their broad powers vested by the Philippine Constitution to adopt tobacco control policies intended to promote the general welfare, and the health, safety, and quality of life of its inhabitants. Increased use of mass and digital media has helped develop a political culture resistant to tobacco industry interference.

Results and lessons learnt: The different LGUs surveyed provided proof that tobacco industry representatives have conducted activities for the following purposes: 1) weaken initiatives to adopt tobacco control local legislation; 2) increase favor with local government officials as part of 'doing business'; and 3) prevent the enforcement of existing laws and policies. The best

practices conducted to counter these activities include: 1) raising awareness about tobacco industry interference through training, community outreach, and media use; 2) developing policies in partnership with the Department of Health, Civil Service Commission and civil society; and 3) denormalizing so-called CSR of tobacco companies.

Conclusions and key recommendations: Political will to protect and promote health from the commercial and vested interests of the tobacco industry is the greatest deterrent to bureaucratic interference. Tobacco control training programs sponsored by Johns Hopkins School of Public Health, World Lung Foundation, the Department of Health, Civil Service Commission, and local civil society organizations have been instrumental in shaping a new kind of political leadership in the Philippines.

PD-754-27 Sustaining tobacco control under tobacco industry surveillance in Chandigarh, the first smoke-free city in India

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Background: Chandigarh (city beautiful) with population of 1.05 million, a Union territory in north India, is the capital of Punjab and Haryana states. Tobacco control became a national mandate with notification of the smoke free rules in 2008. An aggressive campaign led by the Burning Brain Society (NGO) with health authorities raised the profile and Chandigarh became the first Smoke Free City in India in 2007, reducing the prevalence of tobacco use to 14% in 2008-2010. Financial support from Government or any agency is still awaited.

Challenges: The tobacco industry was stunned by smoke free and tried to persuade Chandigarh Administration to allow smoking zones in the city. They started Red and White bravery awards in 2009 and Godfrey Philips awards 2011 to attract social workers across India. Promoting tobacco through schools (free distribution of copies and geometry boxes) in 2012 followed hookah bars opening and sponsoring junior national tennis cup to attract youth.

Intervention: Some challenges were anticipated and rest were addressed with time. All the violations were reported in the tobacco control cell in collaboration with NGO and finally moved to the court of law through police in public interest. Article 5.3 of the FCTC was explored to stop industry interference. Big celebrities were panelised under the law ensuring huge media coverage.

Results and lessons learnt: Chandigarh has successfully maintained the status of Smoke free and set an example for tobacco control in the country. Banning e-cigarette, closing hookah bars and banning sales of single cigarettes are the latest innovations. Studies show effective regulation with substantial decrease in tobacco use in Chandigarh.

Conclusions: Effective tobacco control invites more attention of the tobacco industry. A vigilant system in place can counter and address the emerging challenges.

PD-755-27 Judicial interventions as the most effective tool for countering tobacco industry interference: lessons from Mandi District in Himachal Pradesh, India

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Background and challenges: Indian tobacco control law (COTPA 2003) provides a ban on smoking in public places, protection to minors (<18 years) from tobacco, a TAPS (Tobacco advertisement, promotion and sponsorship) ban and specified health warnings on packets containing tobacco. The tobacco industry violates the TAPS ban, by targeting youth to increase the demand. According to Indian law all cases of TAPS shall be produced in the court but the proceedings are complex. The concerted efforts of the District health authorities and NGOs in Mandi District of Himachal Pradesh in India succeeded in penalising the violators through court cases, ensuring an effective TAPS ban.

Interventions: A team of trained officers with an NGO started the campaign to remove all point of sale advertisements through awareness notices to the owners of the premises in 2012. The remaining boards of direct and indirect advertisement of tobacco were seized as per law. The tobacco companies started promoting use tobacco through prizes, gifts in schools and communities but the all tobacco promoting items were taken in possession. All cases were presented in the court as per the procedure under law after collecting favourable evidences.

Results and lessons learnt: In spite of the huge opposition by the tobacco industry in the court the much needed judgments came on 15 November 2014 and 5 December 2014 in which the accused were panelised under Section 5 of the COTPA 2003 (the punishment is imprisonment up to 2 years and a fine up to Rs 5000, or both) for tobacco advertisement and promotion. The judgements were highlighted in the media for wider publicity, which resulted in 83.26% compliance of the outdoor advertisement ban in the District as per the compliance assessment survey report 2015.

Conclusion: Indian tobacco control law has an enormous scope to combat TAPS. Courts have the mandate to favour public interest but all proceedings shall be as per the procedures within the existing laws.

PD-756-27 Innovative approaches to counter tobacco industry interference in sustaining tobacco control: lessons from the state of Himachal Pradesh, India

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Background: Himachal, a northern hilly state having population of 6.7 million is a famous tourist destination in India. The prevalence of male smokers (33.4%) in the state is more than the country (24.3%) with high passive smoking exposure (79.2%) to non smokers at homes (source, GATS 2009–2010). Achieving Smoke free

Shimla city in 2010 followed Tobacco industry encounters by setting cigarette production units in rural villages (claiming employment to 150 000 women), surrogate advertisements and illicit trade of tobacco. Following smoke free Himachal in 2013, the Industry approached the High Court with the argument that the state is losing tobacco taxes of 13 million INR yearly due to tobacco control. The industry started multiple tobacco promotional activities through schools and lifetime achievement awards too.

Interventions: Advocacy by the local NGO (HPVHA) in partnership with the state Health department resulted in the notification of State and District level committees for monitoring the tobacco industry in 2009. Law enforcers were incentivised to utilize the fine collected under tobacco control for anti tobacco activities. Scientific evidences were gathered against tobacco manufacturing units to sensitise the main stakeholders. NGOs were empowered to issue awareness notices to the violators. In addition to NGOs and media, a Toll free number was started for reporting violations by general public. Tobacco control advocates were rewarded to boost their moral. The school teachers were authorised to stop sale of tobacco near educational institutes. All 3400 gram Panchyats passed resolutions supporting tobacco free villages.

Results and lessons learnt: Himachal became a smoke free State in 2013. 197 225 USD have been collected as fines and utilised for tobacco control up to 2015. All the cigarette production units have been closed. The industry argument for not selling the products in the state was neutralised with indirect harms. Ban on sales of smokeless tobacco, ban on sale of single cigarette and now licensing tobacco vendors are the latest innovations. Fine and imprisonment for tobacco advertisements, illegal trade of tobacco and tobacco promotional activities has happened through courts judgements.

Conclusions: Innovative approaches are much needed for countering tobacco industry interference provided, such innovations shall be sustainable.

PD-757-27 'Loose ends' in compliance with ban on 'loose cigarette' sales: a descriptive analysis of tobacco vendors at point of sale in India

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Background: Raising retail tax is one of the most effective means to reduce tobacco use and encourage smoker to quit, while sale of loose cigarettes may prevent effective implementation of such taxation. World Health Organization's (WHO) Framework Convention on Tobacco Control (FCTC) recommends countries to eliminate sale of kiddie packs and single sticks, many countries have not adopted this as a policy including India. In 2015, Government of Punjab had banned the sale of Loose Cigarettes, it being a violation of Section 7

of Cigarette and Other Tobacco Products Act (COTPA). Under this section, there should be mandatory pictorial health warnings on tobacco products. The study was conducted to monitor awareness and compliance of tobacco vendors regarding ban on sale of loose cigarettes in Punjab, India.

Methods: This cross-sectional descriptive study was carried out among 300 randomly selected tobacco vendors at Point of Sale (POS) in three districts of Punjab, India which represents three major regions of the state. A semi-structured interview schedule and an observation checklist were developed, mainly containing questions related to knowledge and compliance to ban on sale of loose cigarettes. The ethical permissions from state government and Institute Ethics Committee were obtained for conduct of study.

Results: Almost 45 % of vendors, 46% in urban areas and 42% in rural areas, were aware about the recent ban on loose cigarettes. 88.7% of vendors were not complying with the recent ban and were found selling loose cigarettes. Most (95%) of them were however supportive of the ban. The vendors however voiced their view that legislation should be strictly implemented across vendors in the state.

Conclusion: Despite moderate awareness about the recent legislation banning the sale of loose cigarettes among tobacco vendors, very low percentage were found to be compliant to ban on sale of loose cigarettes. Stronger enforcement drives are required for effective compliance of the ban.

PD-758-27 Illicit tobacco products: tobacco industry in disguise to weaken the impact of pictorial warnings

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Background: Health warnings on tobacco packs have been found to inform users about the health hazards of tobacco, encourage users to quit, and prevent non-users from initiating. But tobacco companies always resist the policy implementation of PWS and make efforts to derail the process. To understand the issue, an assessment by way of a structured interview and tobacco product sampling was carried out in January 2016 to assess the tobacco industry's compliance to the mandatory pack warnings and their resistance to related legislations in the State of Punjab.

Methods: A total of 300 point of sales were visited and a random sample of 1500 tobacco products, 5 from each vendor were examined, covering cigarettes, bidis, and chewable tobacco products, to assess the parameters like size of the PWs; placement on the pack, clarity ; and language of PW. A basic interview questionnaire was also filled from 300 vendors to assess qualitative aspects of the survey

Results: Out of the 1500 products examined 525 were Indian made cigarettes; 484 were illicit/ imported cigarettes; 240 were bidi samples and remaining 251 samples were chewable tobacco products. The 525 Indian made cigarettes had PWs. 100% of the illicit/ imported cigarettes constituting 32% of the sample, didn't have any PWs; the packets were without manufacturing/expiry dates; name and address of the manufacturer/importer. Out of 240 bidi samples; 54 (22.5%) had diluted PW, which were either not readable; or placing of the same was inappropriate, colour scheme of the same merged with that of the PW, hence diluting the PWs and similarly 72 samples (28.68%) of the chewable tobacco products were without proper PWs. 65% of the vendors admitted that the wholesalers and suppliers pushed the illicit /imported cigarettes and claiming them to have high margins.

Conclusions: Major Indian cigarette companies complied with the law but presence of huge illicit tobacco products without PWs is a matter of concern. Compliance by bidi and chewable tobacco companies was poor to moderate and needs to be strengthened. Illicit Tobacco Products are weakening the impact of PWs. Compliance of the PWs is alarmingly being weakened by Illicit/Imported Tobacco products.

16. TB diagnostic pathways: improving its steps

PD-759-27 Sputum sample transportation system for DR-TB diagnosis and treatment follow-up of DR-TB patients

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Background and challenges to implementation: Access to DR-TB (drug resistant tuberculosis) diagnosis and treatment follow up remains a challenge in Bangladesh and adversely affects DR-TB treatment. Many presumptive DR-TB patients don't have access to diagnostics, and follow up culture tests of DR-TB patients on community based treatment is often not done or is delayed due to distance from services and socio-economic factors. The objective of this study was to determine the number of TB and DR-TB cases detected and follow up cultures performed following introduction of a sample transportation system.

Intervention or response: Challenge TB Bangladesh supports the sputum sample transportation system through courier in 19 districts and three cities. Kits were provided to local health facilities for collecting and sending samples by courier to the nearest reference

laboratories. Samples were processed with cetylpyridinium chloride for follow up culture; for diagnosis, sputum was sent for Xpert MTB/RIF testing. Data were collected between January 2015 and December 2015.

Results and lessons learnt: 2152 samples from 661 presumptive DR-TB patients and 476 DR-TB patients on treatment were transported by courier; 9 follow up samples were discarded due to lack of necessary information. Of these, 1482 samples from 476 DR-TB patients on treatment were inoculated for culture at NTRL Dhaka and RTRL Chittagong. Of these, 121 (8%) were positive. Among 661 samples, 269 (41%) TB and 28 (4%) DR-TB cases were diagnosed. Estimated cost per courier is around \$1, compared with patient travel costs around \$25. Average time for sample transportation was 2.5 days. The findings are promising for the NTP to improve cost-effectiveness of diagnosing TB patients by Xpert MTB/RIF and ensuring timely treatment follow up testing of DR-TB patients. Coverage gaps in the courier system were a challenge; this was overcome through the use of implementing partners' staff to transport samples to the district/sub-district level.

Conclusions and key recommendations: The sputum sample transportation system is a cost effective and replicable mechanism, increasing patients' access to diagnostic and follow up testing, and decreasing patients' inconvenience and out-of-pocket expenditure. This system can contribute to increased detection of DR-TB cases.

PD-760-27 Evaluation of OMNIgene SPUTUM (OM-SPD) reagent for the transport of clinical specimens to a reference laboratory without cold chain

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Background: Despite great advances in tuberculosis (TB) diagnostics, most tools are intended to be used in higher level laboratories. In this context, it is essential to preserve the quality of specimens during their referral to the testing site. Several companies are developing products that retain the viability of TB cells in specimens without cold chain. DNA Genotek Inc. (Ottawa, Canada) has recently developed OM-SPD to liquefy and decontaminate sputum samples allowing their transport without cold chain.

Methods: We evaluated the effectiveness of OM-SPD for the recovery of viable *Mycobacterium tuberculosis* in sputum samples compared to the standard NALC/NaOH decontamination and secondly the capacity of OM-SPD to stabilize nucleic acid prior to molecular testing. Thirty-two (32) smear positive sputum specimens were collected at the National Reference Laboratory (NRL) Tirana, Albania. Each sample was divided into two aliquots, one was decontaminated by NALC/NaOH method, whereas the second was treated by OM-SPD.

While NALC/NaOH decontaminated samples were immediately inoculated in BACTEC MGIT 960 tubes, the ones in OM-SPD were kept at ambient temperature and sent to the Supranational Reference Laboratory (SRL) Milan, Italy, at various times for further processing (i.e. liquid culture and molecular testing).

Results: We showed that *M. tuberculosis* cells remain viable in OM-SPD treated samples up to 14 days at room temperature. At the time of analysis, 22/32 (68.8%) OM-SPD treated samples were culture positive (average time to positive -TPP- result 14.4 days) as compared to 20/32 (62.5%) NALC/NaOH treated ones (average TPP 10.8 days). For the remaining negative samples culture is still ongoing. Notably, the rate of contamination for liquid culture decreased from 25% to 0% when samples were treated by OM-SPD as compared to NALC/NaOH. DNA extracted from specimens preserved in OM-SPD was tested by PCR giving an interpretable result in 100% samples. A second phase of this validation study is underway to confirm and further expand these results to smear negative samples.

Conclusions: OM-SPD is a very promising reagent for the preservation of sputum specimens at ambient temperature which is particularly relevant in contexts where the sample referral system is weak and the maintenance of cold chain is challenging.

PD-761-27 Improving sample transport to drive service delivery in TB care

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Background and challenges to implementation: As in many high-burden TB countries, the existing national sample transportation (ST) network in Ethiopia is fragmented in terms of couriers, transportation modes and funding, and the lack of a common framework for understanding the scope and costs of the network make difficult to establish an integrated and optimized service model. This can improve cost efficiency but more importantly improve patient outcomes. A suboptimal ST system can hinder timely testing, results delivery and treatment initiation for TB (and all) patients in critical need.

Intervention or response: The CHAI ST project in Ethiopia aimed to generate a clear understanding of the national ST system needs, clarify the scope of those services and determine the interplay those elements and the cost. Three components were developed in order to reach a mutual understanding of the total network costs per year: the referral route distance, the network cost per km, and the frequency of sample collection. This analysis re-invigorated the discussions between Ethiopian Public Health Institute (EPHI) and the Ethiopian Postal Service (EPS) on a national ST system to be rolled out.

Results and lessons learnt: The route analysis indicated the network was in excess of 370 000 km. The network cost per kilometer was developed through direct cost driver analysis and was estimated at \$0.44 per Km for car-based service and \$0.57 per km once costs associated

with the routes network were taken into account. The biggest impact on total network costs was the frequency of sample pick-up, each time requiring the complete national network distance to be covered. The country adjusted this optimal frequency based on different sample types. Given the significant budget requirement of fully-serviced network the team has also developed scale-up scenarios by prioritizing certain sites for the first phase.

Conclusions and key recommendations: Discussions between EPHI and EPS have resumed as a result of the analysis. They plan to continue negotiations and will discuss the scope and timing to scale-up the network. We believe similar analysis can be of value in optimizing the use of resources and patient impact in other countries.

PD-762-27 A meta-analysis comparing different sputum collection methods

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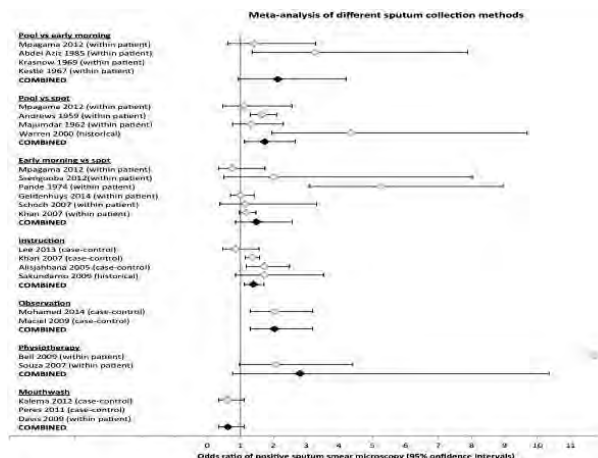
Background: The diagnostic yield of laboratory tests to diagnose tuberculosis disease is dependent on the quality of the sample. The relative merits of methods to obtain adequate quality samples from people suspected of having tuberculosis are poorly characterized. Although procedures such as bronchoscopy and sputum induction may have value, they are often unfeasible in the resource-constrained settings where most tuberculosis occurs.

Response: A systematic review and meta-analysis was performed to assess if any sputum collection technique was superior in improving tuberculosis diagnostic yield with microscopy and culture. Several databases were searched between 24–28 June 2015 for publications comparing non-invasive sputum collection techniques. 22 studies were identified, involving 10 387 samples. These were analysed concerning 7 distinct research questions including meta-analyses with a random-effects model. The Cochrane Q test was used to assess heterogeneity.

Results: The studies varied greatly in participants recruited, number of samples collected per study arm, and sample processing. Pooled collection of sputum yielded higher odds of a positive result compared to the standard spot collection for tuberculosis microscopy (odds ratio, OR 1.7, $P = 0.01$) and culture (OR 1.7 $P = 0.01$). Although there was a trend towards higher odds of a positive result for early morning collection vs. standard spot samples, this was not statistically significant for microscopy (OR 1.5, $P = 0.1$). Giving prior instructions or observing the sample being collected improved microscopy yield (OR 1.5, $P = 0.001$) but had no effect

on culture positivity ($P = 1.0$). Physiotherapy-assisted sample collections tended to improve microscopy diagnostic yield (OR 2.8, $P = 0.1$), but there were only two studies.

Key recommendations: Tuberculosis microscopy results are influenced by sputum collection methods more so than culture. Thus improvements in sputum collection techniques should be particularly emphasised in settings where tuberculosis diagnosis is dependent on microscopy.



PD-763-27 LED microscope giving better results in Bangladesh

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Background and challenges to implementation: Smear microscopy is the baseline diagnostic tools for the diagnosis of tuberculosis in Bangladesh. Keeping in mind the possibility of missing low grade TB in sputum smears, NTP Bangladesh has taken a policy to replace conventional microscopes by LED microscope gradually and already replaced it in the 300 TB Laboratories over the country. We conducted an assessment of randomly selected 45 LED sites to measure changes in positivity rate and other pertinent indicators.

Intervention or response: 45 Microscopy centers are selected randomly from who used conventional microscope in 2013 and using LED Microscopy since 2014. Laboratory data of same quarter before and after introducing LED are collected from each laboratory, third quarter of 2013 (ZN staining) and third quarter of 2014 (AO staining). Data are categorized as 'Suspect samples' and 'Follow up samples'. Total number of slides checked from both categories and positive among them are counted. Data is shown as positivity rate for Suspect & Follow up separately and compared between before and after LED.

Results and lessons learnt: Positivity rate among suspect increases in 36 centers, remain same in 3 centers and decrease in 6 centers among 45 sample site. Follow up

positivity rate increases in 37 centers and decrease in 8 centers. In general there is an increase of Positivity Rate among Suspect by 0.8% and among Follow-up by 0.4% which is very significant.

Conclusions and key recommendations: The preliminary result of the initiative shows that LED Microscope could identify missing bacilli and help to diagnose missing TB case as well as early diagnosis of MDR-TB in Bangladesh. Increase in follow up positivity rate indicated early diagnosis of unfavorable outcome and will lead to early diagnosis of MDR-TB. Also, LED is time saving tool as fewer fields are checked.

PD-764-27 Performance of the Xpert® MTB/RIF assay from fluorescent acid-fast stained slides

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Background: Culture is gold standard for TB diagnosis and susceptibility testing. Decreased yield of TB cultures both due to bacterial contamination and harsh decontamination protocols is a challenge for many laboratories. A proportion of these cases are TB smear positive and a negative culture report is frustrating for both patients and clinicians.

In most smear positive and culture negative cases original specimens have already been discarded and the only available material is on stored slides. To identify a possible solution, we evaluated performance of Xpert MTB/RIF assay from material scraped off the fluorescent acid fast (AFB) stained slides of patient's specimen.

Methods: This cross sectional study was conducted at the Aga Khan University Laboratory, Karachi, Pakistan. 18 AFB stained slides from suspected TB patients stained with Auramine O stain were included in the study. Scraped off material from stored slides was mixed with 0.5 mL of phosphate buffer saline. Xpert MTB/RIF assay was performed from this suspension according to manufacturer's instructions. TB cultures and susceptibility data already available on these cases were used as gold standard.

Results: A total of 18 AFB slides from 18 patients (12: sputum, 4: bronchial wash, 1: tissue, 1: pleural fluid) were included, of which 14 (77%) were smear and culture positive. Of the smear positive specimens, Xpert/RIF assay was positive in 100% of the cases. Rifampicin resistance was found in 2/14 cases and accuracy of detection was 100%. Of the 4 smear negative specimens, Xpert MTB/RIF assay was positive in 1 case. This case was culture negative. Overall sensitivity was 100% and specificity was 75%.

Conclusions: In view of excellent performance of Xpert MTB/RIF assay from fluorescent acid fast stained slides, this technique could be used in situations where AFB smear is positive and TB culture negative and a repeat specimen cannot be obtained.

PD-765-27 An incremental cost-effectiveness analysis of a second Xpert® MTB/RIF test for detecting *Mycobacterium tuberculosis* and rifampicin resistance

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Background: Due to the inhomogeneity of specimens collected from tuberculosis (TB) patients, repeated Xpert MTB/RIF tests can have potential clinical benefits. Therefore, the incremental cost-effectiveness was analyzed for the second Xpert MTB/RIF test to detect *Mycobacterium tuberculosis* and rifampicin (RIF) resistance.

Methods: Two specimens were collected over a week-long period from each of the 198 pulmonary TB (PTB) and 104 extrapulmonary TB (EPTB) suspects. The specimens were subjected to smear, culture, Xpert MTB/RIF assays, while the MGIT 960-based drug susceptibility testing was conducted for all of the recovered isolates. An incremental cost-effectiveness analysis of the serial Xpert MTB/RIF examinations for diagnosis of TB was evaluated.

Results: Among the total 177 Xpert-positive TB suspects, with two sequentially examined specimens, 155 (87.57%) were identified by the first Xpert MTB/RIF assay whereas the additional 22 (12.43%) cases were identified by the second assay. The second Xpert MTB/RIF assay had higher incremental yield for smear-negative specimens than for the smear-positive specimens (23.81% vs. 6.14%, $P = 0.003$). The two Xpert MTB/RIF assays were 100% concordant in RIF resistance detection. The cost-effectiveness analysis showed that the incremental cost of performing a second test is huge: US\$93.40 vs. US \$618.75 and US \$106.12 vs. US \$866.67 for PTB and EPTB respectively at the marketing price in China, and 18.64 vs. US \$123.50 and 21.18 vs. 172.99 for PTB and EPTB respectively at the UNITAID negotiated price.

Conclusions: The second Xpert MTB/RIF assay improved the TB detection, but with an increased cost. For RIF resistance detection, one test was enough.

PD-766-27 Knowledge and associated factors on the Xpert® MTB/RIF assay among TB clinic health workers in Addis Ababa

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Background: Tuberculosis is one of the important leading causes of death in humans and it remains a serious public health problem. Early detection and treatment are the most effective measures for the management of tuberculosis. Xpert MTB/RIF assay is playing a major role in accurately detecting *Mycobacterium tuberculosis* and drug resistance simultaneously in

less than three hours. The diagnostic accuracy of this tool is well documented but there is insufficient evidence on knowledge of health professionals of the tool. This study aims to assess the knowledge of health professionals on Xpert MTB/RIF assay and associated factors in detecting TB/TB drug resistance.

Methods: An institution based cross-sectional study was conducted from 4 April to 5 June 2015, in Addis Ababa that involved 209 healthcare providers working in TB clinics. Structured questionnaire through self-administered interview technique was used to collect the data. Bivariable and multivariable binary logistic regression analysis was used to identify associated factors. Odds ratio with 95%CI was computed to assess the strength of the associations.

Results: Majority, 151 (72.2%) of the participants were nurses by profession of which 119 (79.3%) had Diploma. The overall proportion of respondents who had good knowledge about Xpert was low 96 (46.4%). Health professionals in age range 25–29 years (AOR = 2.9, 95%CI 1.15–7.33) and 30–34 (AOR = 3.46, 95%CI 1.22–9.81), who have been working in TB clinics for more than three years (AOR = 0.351, 95%CI (0.145–0.843) and who read the Xpert guideline (AOR = 0.214, 95%CI 0.116–0.397) were more likely to have good knowledge on Xpert.

Conclusions: This study revealed that the overall magnitude of knowledge status was found to be low. Variables, being young age, reading guideline and being more experienced on TB DOTs clinic work were statistically associated with good knowledge status on Xpert. Distribution of national guideline on Xpert and assigning experienced clinicians in TB DOTs clinics are recommended.

PD-767-27 Experiences and challenges in the scale-up of GeneXpert® services in Oromia and Amhara regions, Ethiopia

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Background: GeneXpert MTB/RIF assay is a novel and automated integrated diagnostic device for the diagnosis of tuberculosis and rapid detection of RIF resistance in clinical specimens. We present the challenges encountered in the implementation of GeneXpert, and the relative improvements made in two regions of Ethiopia.

Interventions: During 1 January to 31 December 2015, a total of 29 345 presumptive TB (HIV positive and children) and presumptive MDR-TB cases were tested by GeneXpert in Amhara and Oromia regions. Routine data was collected from 49 GeneXpert centers from the laboratory log book and GeneXpert machine database. To improve GeneXpert service quality and accessibility, the USAID-funded HEAL TB project provided technical support including regular mentoring, scheduled maintenance, and timely calibration by trained laboratory

personnel. The project also provided an Uninterrupted Power Supply device to address electricity interruptions.

Results and lessons learnt: Out of 29 345 tests processed by the GeneXpert, 2798 (9.5%) were documented as unsuccessful result. The most frequent reason for unsuccessful result was poor sample quality and presence of PCR inhibitor in the sample which accounted for 1109 (39.6%) of cases (invalid). Poor sample processing technique, instrument temperature failure, communication failure with the computer, and lack of cartridge integrity accounted for 1008 (36%) of unsuccessful results (error), while 681 (24.3%) were due to electricity interruption (no result). Unsuccessful results improved over the year: 13.8% reduction in 'error' results related to poor sample quality; 28.1% reduction in 'invalid' results related to technical problems; and 66.8% reduction in 'no result' related to power interruptions. Most of the errors were avoidable by regular preventive maintenance and strict adherence to test procedures.

Conclusion: The rate of unsuccessful results improved over the year. However, it is still higher than the 3% unsuccessful result reported in South Africa. More effort is needed to improve sample quality and the technical aspects that contribute to unsuccessful results.

Table Improved unsuccessful GeneXpert result

	Jan–March 2015	April–June 2015	July–Sept 2015	Oct–Dec 2015
Error (%)	4.35	3.47	2.23	3.75
Invalid (%)	4.49	4.02	4	3.23
No result (%)	4.19	3.97	2.16	1.39

PD-768-27 Optimizing TB diagnosis among PLHIV using GeneXpert® machines through a robust specimen transport and result reporting system using motorbikes

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Background: Despite benefits from the inclusion of GeneXpert machines in the TB diagnostic algorithm of Nigeria National TB Program, these machines remain underutilized with long turnaround times and delay in initiation of TB treatment. The challenges include difficulties accessing the machines as a result of far distance, bad road networks, and poor transportation systems. Previous interventions to address these bottlenecks were mainly targeted at delivery of specimens with a minimal emphasis on result retrieval and quality improvement.

Objective: To describe the processes of utilizing motorbikes to strengthen specimen movement for TB diagnosis among PLHIV, increase utilization of GeneXpert machines and improve turnaround around time for test results in southern Nigeria.

Intervention: The riders of the motorbikes were trained on proper road use, handling of biohazard materials and

data collation and reporting. An entry meeting was held with stakeholders to define roles and develop routing charts. Specimens were transported by the riders to GeneXpert sites for examination and their results were taken back to the referral facilities on specified days. Activities at all levels were meticulously documented daily and summarized monthly and regular follow-up monitoring visits were conducted.

Results and lessons learned: Early results demonstrated an increase in TB screening among PLHIV due to clinicians' confidence about obtaining a result. An increase in the utilization of GeneXpert machines has been reported with 100% of collected specimens successfully processed and their results returned to the referral facilities. The turnaround time for the results has greatly improved, with more than 95% of results returned to the referral facilities within 2 days compared to 6 days prior to the intervention. The quality improvement monitoring tools demonstrated the ability to monitor performance at every stage of implementation.

Conclusions: A robust specimen transportation and result retrieval system equipped with quality improvement monitoring tools can lead to optimization of the use of GeneXpert machines and reduction in the turnaround time of results enabling clinicians to make timely decisions on the management of TB patients. With the capacity built on efficient specimen transportation and result retrieval, there are opportunities for integrated movement of specimens obtained from PLHIV.

PD-769-27 Bacillary burden of tuberculosis measured by Xpert® MTB/RIF and treatment outcomes in a high prevalence HIV setting in Southern Mozambique

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Background: Bacillary burden is an important indicator of disease severity and transmission risk in tuberculosis (TB). The cycle threshold (C_T) of Xpert® MTB/RIF, has shown reasonable correlation with measures of bacillary burden in smear and culture, but evidence is limited in high HIV prevalence settings and in its relation to outcome data.

Methods: Individuals aged 15 and over enrolled in a larger TB study in Manhiça, Mozambique, found to have Xpert MTB/RIF positive sputum had bacillary burden measured by smear grade, time to positivity (TTP) in liquid culture (MGIT) and Xpert C_T . Descriptive analysis, correlation of measures of bacillary burden and effect on outcome data were assessed.

Results: Xpert positive TB was detected in 281 participants. Median age was 35.5 years (IQR 28–46); 21 (7.5%) had a positive or indeterminate Xpert resistance probe. The proportion of participants with HIV was 73.3%. Of those, 96 (55.5%) had $CD4 < 200$ cells/mm³.

Sputum smear was positive in 172 (61.2%) participants; 244 (86.8%) were MGIT positive with median TTP of 7.5 days (IQR 5.0–11.6); median of mean C_T was 19.8 (IQR 15.7–26.6). Bacillary burden was lower among HIV positive participants by all measures. Mean C_T correlated with TTP ($p < 0.001$) and decreased with increasing smear grade (ANOVA - adjusted R^2 0.55, $P < 0.0001$). Correlation was decreased at lower levels of bacillary burden. Mean C_T cut-off for smear positivity was 27.4 with 95% sensitivity and 54% specificity vs. 18.2 with 95% specificity and 60% sensitivity. Of patients with available treatment outcome data, 199 (81.6%) were successfully treated, 32 (13.1%) died and 10 (5.3%) failed treatment. Mortality was associated significantly only with HIV positivity ($p < 0.021$); treatment failure was associated with higher bacillary burden among all measures (mean C_T $P = 0.009$, TTP $P = 0.039$, smear grade $P = 0.007$).

Conclusions: This study adds to the evidence that Xpert C_T correlates with traditional measures of bacillary burden. As Xpert is rolled out worldwide, C_T could prove to be a useful surrogate for smear status in assessing transmission risk. Whilst there were few participants with treatment failure, this study provides preliminary data to warrant further investigation of the association between C_T values and treatment failure.

PD-770-27 Cost-effective and innovative technology for effective and rapid TB response in Nigeria

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Background and challenges to implementation: Nigeria is ranked as the 3rd highest TB-burden and 11th DR-TB burden country in the world according to 2014 Global TB report. The country relies on genexpert for MTB/RIF Resistance diagnosis but reporting TB testing results is a lengthy process due to a continued reliance on paper records and slow data transit systems. Quality of results data is often poor and subsequent program management decisions are not always timely.

Intervention or response: Abt Associates and SystemOne developed an innovative cost effective mobile-based technology that sends diagnostic results in an SMS alert to key TB program managers/DR-TB enrollment officer instantly from Genexpert machine to enable quick enrollment of newly diagnosed patients in treatment and ensure effective and rapid response. GxAlert is configured on GeneXpert systems by installing a router that sends encrypted data sent to the secure web-based GxAlert database in real time.

Results and lessons learnt: The proportion of DR-TB patients enrolled for treatment based on GxAlert messages received from 35 GeneXpert facilities jumped to 85% in March, 2015 from only 50% enrolled in April 2014. Program manager now receive SMS or text

message alerts to speed treatment initiation. Weekly reports of all new TB+ cases are both emailed and sent by SMS to local health officials to ensure better connection between diagnosis, enrollment and treatment. With this excellent foundation set for national-level reporting and response.

Conclusions and key recommendations: GxAlert has demonstrated its potential to strengthen surveillance of DR-TB, TB in children and the HIV infected, speeding response and improving programmatic decision in over 90 labs through the National TB Program (NTP), reporting tens of thousands of test results making for faster enrollment of patients in treatment programs. This innovation has made it possible to get diagnostics results immediately back to clinicians and patients; identified \$100k of commodities that would expire before use; led to immediate reallocation and redesign of NTP logistics unit approaches to GeneXpert supplies, identified MDR strains variation by region, enhanced site selection, diagnostic machine utilization, and machine uptime and improved adherence to maintenance regime (calibration and module replacement).

17. TB among refugees

PD-771-27 Addressing cross-border control of tuberculosis among labor migrants in Kazakhstan

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Background: Kazakhstan is experiencing a rapid economic growth and a large influx of migrants from neighboring countries in the Central Asian region. The burden of MDR-TB remains one of the region's greatest public health challenges.

Since December 2014, a project is being implemented and aimed at prevention and TB treatment among migrants under a grant funded through the GFATM New Funding Model. The project is being implemented in seven pilot sites in Kazakhstan.

Intervention: The activities under the project are directed at: 1) removing barriers that restrict access to TB services for migrants; 2) providing TB prevention and treatment services among migrants; 3) strengthening engagement of community systems and enhancing the role of civil society and non-governmental organizations in provision of TB control and support to migrants.

Results: In the first year of the project's implementation, the following activities have been conducted: 1) over 300 staff members from NGOs and healthcare facilities have been trained at 14 trainings; 2) since July 2015, a contract has been executed with five local NGOs for implementation of outreach and information campaigns, as well as provision of social support to migrants in Kazakhstan with incentives distributed; 3) a network of

'friendly' general healthcare and TB facility partners has been identified for migrants access to TB diagnostics and treatment. From July to December 2015: 1) 11 991 migrants received information about TB symptoms and project activities; 2) 1369 migrants were examined for TB, including X-ray screening; 3) 13 migrants received a diagnosis of confirmed TB. To enhance partnerships with national TB programs, a high-level regional meeting has been held to discuss cross-border TB control in the Central Asian region. The meeting developed a 12-month work plan for execution of bilateral /multilateral agreements on TB control between Central Asian countries.

Conclusions: TB diagnostics and treatment activities require engagement of government institutions, and NGOs in order to ensure partnerships and synergies in the area of TB detection and treatment among migrants. Therefore, TB screenings and awareness campaigns on TB symptoms, as well as access to TB diagnostics and treatment need to be provided to this high-risk group.

PD-772-27 Yield of tuberculosis among immigrant populations: lessons from Kyangwali refugee camp in Uganda

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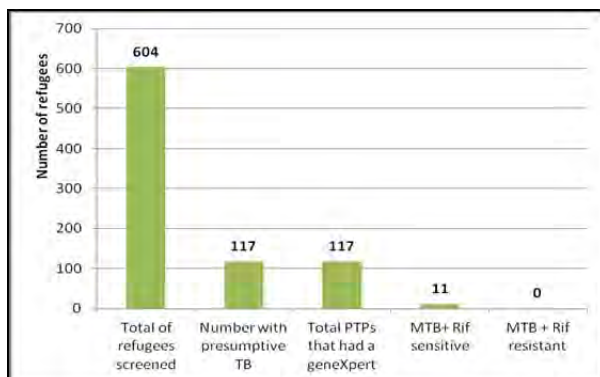
Background: The risk of transmission of tuberculosis (TB) among immigrants remains high as they are predisposed to crowding, challenges of accessing health care and completing treatment. The Kyangwali refugee camp in Hoima Region is host to 25 000 refugees from DRC and South Sudan. The camp is served by two low level health centers with inadequate capacity for diagnosis and treatment of TB. There is no routine screening for Tb among refugees. One of the patients being treated for multidrug resistant TB (MDR-TB) at Hoima Regional Referral Hospital (HRRH) was found to be a resident of Kyangwali refugee camp.

Intervention: HRRH with support from the USAID-funded TRACK TB Project conducted contact screening and investigations in the camp. The camp authorities were sensitized to mobilize other refugees for health education and TB screening through engagement of Village Health Teams. The refugees were screened for TB using the Intensified Case finding form and all presumptive TB (PTP) cases were subjected to an MTB/RIF test.

Results: A total of 604 refugees (397 F and 207 M) were screened for TB. All were adults and older children who could produce sputum. One hundred and seventeen (19.4%) PTPs were identified and had their sputum samples subjected to the MTB/RIF test. Eleven PTPs (9.4%) were diagnosed with drug sensitive TB; three (27.3%) of these were women and none of the diagnosed

patients had rifampicin resistance as shown in the Figure. Results show a 10-fold equivalent to the estimated prevalence of TB in the general population.

Conclusions: The prevalence of undiagnosed TB in refugee settings coupled with predisposing social conditions and limited access to health care services increase the risk of transmission and could undermine TB control efforts in the host communities. We recommend strengthening of regular TB screening, diagnostic and treatment services for immigrant populations in camp settings.



PD-773-27 TB prevention and care in five Tibetan settlements in India: a community perspective

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Background: Tuberculosis (TB) continues to be one of the biggest public health challenges in India and TB incidence in Tibetan refugees is substantially higher than the native population; nearly 30% of the Tibetan refugees living in India were infected with TB, with high incidence of multi-drug resistant TB (MDR-TB). It is important to reduce the large pool of latent infections, high incidence of TB and emergence of drug resistant TB among Tibetan refugees. This paper explores the health seeking behaviour of TB among these communities and their perspectives.

Methods: Out of all 39 Tibetan Settlements in India, four of the large and one medium size Tibetan Settlement were selected. The local school, monastery and nunnery, community members, community leaders were identified and 30 Focus Group Discussions conducted. Thirty in-depth Interviews were conducted among randomly selected Patients in Health Facilities. Written consent was obtained from participants before and Ethical approval sought. Responses were analysed under different themes and data triangulation were carried out.

Results: Among the Tibetan refugees, students and monks/nuns are more vulnerable to TB, specifically living in congregate settings. Awareness of TB symptoms

is high among all groups but knowledge on treatment adherence and nutrition is low. Community leaders are well connected and also help in awareness generation on TB and access to services. Monks and Nuns were mostly attributed incidence of TB to hardships and lack of nutrition. School children mentioned school nurse as 1st point of referral and reported about TB awareness programs in school. Students also reported about annual TB screening and being tested for contact tracking for TB. Majority of MDR-TB patients are aged below 25 and work in restaurant, are a sweater seller or student. They are under DOTs and most of them recalled to have TB earlier. Almost all of them reported on contact with another TB patient before being diagnosed.

Conclusions: TB Awareness is high but treatment adherence is low. Most of the TB cases were due to contact transmission and living under congregated settings. More focus is needed on prevention of transmission of TB and regularized TB screening, especially for people living in congregated settings.

PD-774-27 Combination of active case finding and contact screening: high yield in a residential school for Tibetan refugee children in India

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Background and challenges: Tuberculosis is major public health challenges among Tibetan refugees in India. 53.5% of them who live in congregate settings, in monasteries, nunneries and residential schools have increased risk of TB transmission.

Intervention or response: The Tibetan Government in Exile conducts Active Case Finding (ACF) for TB in all its schools, every year. In 2015, in TCV School, Suja, students were screened using a step-wise protocol, which included symptom questionnaire, clinical examination, chest X-rays and CBNAAT.

The contacts of 6 TB cases, including 1 MDR, who were diagnosed on the basis of ACF, were further screened and 4 more TB cases, including 3 MDR were diagnosed amongst them. Incidentally all 4 cases, diagnosed through CS, were also identified for ACF and had negative chest X-Rays, therefore CBNAAT was not done for them during ACF. Their TB was confirmed only when they were reviewed again and their CBNAAT was done during Contact Tracing.

Results and lessons learnt: Students and staff 1528; Persons undergoing clinical screening for ACF 331; TB cases diagnosed by ACF 6 (4 New, 1 Relapse, 1 MDR); Persons undergoing clinical screening for CS 137; TB cases diagnosed by CS 4 (1 New, 3 MDR); Chest X-Rays done 186; CBNAAT tests done 57; Proportion of screened persons having TB (ACF) 6/331=1.81%;

Proportion of screened persons having TB (CS) 4/137 = 2.91%; Number Needed To Screen to detect 1 TB case (ACF) 55; Number Needed To Screen to detect 1 TB case (CS) 34; Approximate cost of investigations INR 1250 for CBNAAT and INR 250 for chest X-Rays, INR 117 750 or USD 1707.

Conclusions: 1) A combination of ACF and CS yielded 10 TB cases, including 4 MDR, among Tibetan students living in congregate settings; 2) Including CBNAAT in screening protocol promoted better pick up of drug sensitive and drug resistant cases; 3) Approximately 171 USD were needed to identify 1 TB case; 4) Annual ACF combined with aggressive CS, whenever a TB case is diagnosed, is a good practise for Tibetan refugees living in congregate settings. Inclusion of CBNAAT in ACF protocol is justified in such highly vulnerable populations.

PD-775-27 Cross-border migration of MDR-TB patients between Equatorial Guinea and Cameroon: a solution through South-South collaboration

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Background and challenges to implementation: The Cameroonian NTP has been successfully treating MDR-TB since 2005. In 2015, the NTP was challenged by a massive influx of patients from neighbouring Equatorial Guinea (EG), a country not diagnosing nor treating MDR-TB. Available resources came under stress; questions rose about the extent of the MDR-TB problem in EG and reason behind; additionally, some EG patients presented a pre-XDR (Quinolones) resistance profile. Questions rose, finally, how to tackle in a joint country over-bridging effort the challenge.

Response: Stepwise, the following actions were undertaken: 1) The Cameroonian NTP proposed to the EG counterpart a joint exploratory mission - financed by The Union - to evaluate the extent of the MDR-TB problem. 2) Observing a back-log of about thirty untreated MDR-TB patients in EG, WHO and the two MOHs were informed. 3) A second joint mission, commissioned by WHO, described the epidemiological situation, evaluated the NTP's performance, and elaborated a time-framed and budgeted emergency plan of action. 4) A Memorandum of Understanding (MoU) between the two countries proposed for a transitional period of two years: a) EG samples all MDR-TB suspects, Cameroon realizing drug-resistance testing; b) MDR-TB patients continue to be treated in Cameroon; c) Personnel from EG is trained in Cameroon d) A treatment unit is identified in EG; e) Trained EG personnel receive patients in their continuation phase, monitored by Cameroon; f) EG orders laboratory material and MDR-TB drugs and starts a comprehensive MDR-TB control program monitored by

Cameroon; and g) EG improves NTP performance, updates recording and reporting system.

Results and lessons learnt: After nine months, 28 (75%) EG retreatment cases were tested; 17 MDR-TB cases identified, nine started treatment; GeneXpert device and drugs about to be delivered; a structure for treatment identified, four personnel trained, 4 patients on follow-up treatment in EG. · Main difficulty consists in mobilizing (principally available) funding.

Conclusions: A comprehensive situation analysis, technical sound proposals (based on Cameroon's experience), strategic plaidoyers towards and subsequent pragmatic decisions by partners (The Union), the WHO, and Governments can result in quickly established, effective, promising South-South collaboration for tackling emerging common health problems.

PD-776-27 The yield of screening campaigns for tuberculosis in camps of internally displaced people in Iraq

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Background: Tuberculosis (TB) is endemic in Iraq with an estimated incidence of 43/100 000. Increasing access of TB care services to vulnerable groups is crucial for TB control. After 2003, Iraq underwent two large waves of internally displaced populations (IDPs) due to brutal violence. The Anti-Tuberculosis and Chest Diseases Society in Iraq (IATA) aimed at assessing the yield of screening for TB in IDPs living in camps who are recently displaced compared to IDPs displaced for more than five years.

Methods: During 2013–2014, the IATA conducted screening surveys with mobile X-ray cars and labs to 17 camps of internally displaced people (IDP) (all known large IDP camps in Iraq) with a total population of 49 780. Inhabitants of these camps were displaced during the sectarian events occurred in Iraq during 2005–2007. During screening, the duration of displacement exceeded five years.

During 2014–2015, IATA conducted another screening campaign for all known new IDP camps in middle and southern Iraq occupied by 136 072 people who were displaced after ISIS invasion to a wide area of west and middle of Iraq after 6 June 2014. During screening, the duration of displacement was around one year or less. Sputum examination for AFB and chest X-ray were performed on site using a mobile X-ray and laboratory vehicle; other more sophisticated investigations were done in nearest public hospital to the camp.

Results: The first screening campaign yielded examining 1828 patients (3.7% of the targeted population). Out of the examined patients, 41 (2.2%) were diagnosed to have TB including 38 (2.1%) new TB patients. The rate of newly detected TB patients out of the targeted population was 63.6/100 000.

The screening of new IDPs camps resulted in examining 3089 (2.3% of the targeted population). 14 (0.5%) TB patients were detected including 12 (0.4%) new TB cases. The rate of detecting new TB cases was found 8.8/100 000. The likelihood of detecting new TB cases by active case finding campaigns in IDPs camps increases to 7 folds if the duration of displacement is long.

Conclusion: Active TB case finding campaigns in IDPs camps have a good yield in condition of long displacement.

PD-777-27 Novel case management strategy for latent tuberculosis infection among migrant farmworkers

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Background and challenges to implementation: An estimated two billion people, approximately one-third of the world's population, have latent TB infection (LTBI). Our previous work has shown high LTBI prevalence (~60%) among migrant farmworkers from Mexico in Arizona. However, limited access to health-care and health insurance, language barriers, poor education, long working hours, and political, social and economic disenfranchisement make follow-up care and treatment difficult for a potential illness.

Intervention or response: As part of a broader project screening farmworkers for LTBI at the Arizona-Mexico border, the Migrant Clinicians Network (MCN) contracted with the University of Arizona to provide follow-up services, including database management, tracking and phone calls to a cohort of individuals tested for LTBI, with the goal of providing patient navigation as well as case management to any participant for whom treatment was initiated.

Results and lessons learnt: Based on diagnosis of LTBI by either blood or skin test, eighteen participants were directed to the Health Network (HN) project of MCN and a case file was initiated for each one. Every participant was assigned to an HN caseworker. To date, of the 18 test participants, three did not have viable contact information, three participants were lost to follow-up (i.e., no phone number, lack of reports) and communication has been maintained with twelve of the participants. Some challenges to enrollment were absence of a consistent telephone signal, and limited time to explain to the subjects the benefits and limitations of enrollment in HN. Communication represents the key challenge to follow-up for this highly mobile population.

Conclusions and key recommendations: We believe that a shift in focus to tuberculosis prevention is necessary, including diagnosis and treatment of LTBI. While still in progress, our novel follow-up strategy for an at-risk cohort provides important proof of concept of both challenges and possible strategies to follow-up a migratory population. The project was determined to be highly

cost effectively in recently published results. We will continue enrollment into the cohort through 2016.

PD-778-27 TB care in emergency context: Syrian refugees in Jordan and Lebanon

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Background and challenges to implementation: The National Tuberculosis Programmes (NTPs) of Lebanon and Jordan face challenges hosting large numbers of Syrian refugees requiring access to TB services. There are 1 067 785 registered Syrian refugees in Lebanon and 639 734 in Jordan, with many more unregistered (UNHCR Feb2016). The majority of refugees live with host communities, scattered across the countries, frequently changing their location. TB diagnosis, treatment and follow-up are complicated even more by the insecurity/inaccessibility in areas near the Syrian border. The National Tuberculosis Programmes (NTPs) of Lebanon and Jordan face challenges hosting large numbers of Syrian refugees requiring access to TB services.

Intervention or response: Assistance to NTP TB centers with essential diagnostic equipment (e.g., Xpert), consumables, drugs and additional staff is needed in order to address the increased caseload. TB awareness rising and active case finding (ACF) in informal refugee settlements/camps, hard-to-reach areas, and in urban communities by Community Health Volunteers (CHV) and Mobile Medical Unit (MMU) is ongoing. Mobile X-ray units screen refugee populations in hard-to-reach areas. The IOM facilitates referrals, diagnostic tests and hospitalization.

Results and lessons learnt: 140 Syrian refugees with TB were diagnosed in Lebanon in 2015 (only 110 in 2014), while 60 TB cases were diagnosed in Jordan. The ACF contributed to increased case detection (e.g. 19 TB cases detected in Lebanon out of 120 842 screened while in Jordan 30 TB cases detected out of 24 903). CHVs and MMU were essential in reaching out to refugees living in hard to reach areas. The WHO and IOM have taken an initiative for cross-border notification and referral agreement to promote continuity of TB treatment in coordination with the NTPs.

Conclusions and key recommendations: The outcomes confirm that extensive collaborative efforts of the International Community and the NTPs, with funding support (GF Emergency Grant) leads to successful TB control programme in a humanitarian emergency context. Joint innovative approaches are essential to increase TB case detection, reducing morbidity/mortality among displaced/ mobile populations.

Table Treatment outcome of 2014–2015 cohort of Syrian refugees

Country	Patients <i>n</i>	Success %	Mortality %	Lost to follow-up %
Lebanon*	84*	83	5	12
Jordan	104	93	6	1

PD-779-27 Predictors of tuberculosis treatment outcomes in Kakuma Refugee Camp, Kenya, 2015

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Background: Tuberculosis (TB) is one of the leading causes of mortality among infectious diseases worldwide especially in refugee populations. In 2010 there were 8.8 million new cases of diagnosed and 1.45 million deaths worldwide. In Kenya there was an estimate of 90 000 TB cases in 2015 with the mortality rate at 21 per 100 000. The Kakuma camp has an estimated population of 200 000 with majority of refugees from South Sudan and Ethiopia. This study sought to describe the correlates of tuberculosis (TB) infection and TB treatment outcomes among adult and pediatric refugees at Kakuma refugee camp hospital in Kenya.

Methods: We retrospectively reviewed patient records between January 2013 and December 2014 and collected data on patient demographic information, TB diagnosis, and treatment outcomes. A case of TB was defined as bacteriologically confirmed smear positive. Treatment outcomes were categorized as 'improved' if the patient got cured or completed treatment while deaths, defaulters and treatment failures were categorized as poor treatment outcomes.

Results: A total of 88 out of 130 patients with TB had their records reviewed. The number of male patients was greater at 62/88 (70%). The mean age of the patients was 30 years (range 10–68 years) with <14 years (15%) and >14 years (85%). About 28% of the TB patients were HIV positive; 55% tested smear negative while 74% had pulmonary TB. Improved treatment outcome was more likely in pediatric patients in comparison to adult patients (OR = 1.7, 95%CI 1.3–8.1).

Conclusions: Treatment outcomes were better in pediatric patients than adults. Age affects TB treatment outcomes with adults experiencing the worst forms of outcomes. We recommended strengthening of a border surveillance system.

PD-780-27 High non-favorable outcome in districts with significant cross-border interaction: call for regional coordination

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Background: Malawi is a country located in southern Africa sharing borders with Mozambique, Zambia, and Tanzania. In Malawi, a lack of national identity as well as being the only country in this part of SADC which provides health services free to its citizens, have attracted people to seek services from the Malawian health service. Mobility across borders is one of the key factors that have implications in TB control. We reviewed the performance of districts with high cross border activity in Malawi.

Methods: For this analysis, cohorts of 2013 new smear-positive cases were evaluated. Four districts predominantly sharing borders and having wide levels of interaction with neighboring countries were identified. These districts are Karonga, Michinji, Mulanje and Mwanza. The treatment success and loss to follow-up rates were calculated. Comparison was made with national average and the remaining districts. The χ^2 test was done using Epi Info 3.3.4.

Results: Treatment success rate was lower than the national average (80.3% vs. 84%). Districts with mobility across border have higher lost to follow up rate (5.3%) than the national average. The difference were statistically significant.

Conclusions: The movement of patients across border to seek medical care seems to have impacts on desired treatment outcome. This is mainly through inability of the health system to trace and follow up patients on treatment. Countries need to address barriers to TB services so that all patients seek care within their catchment area. National TB control program is using the regional platform to follow up cross border issues.

Table

Category	Number of Cohort <i>n</i>	Treatment success rate %	Loss to follow up rate %	X ² test P value
With cross border activity	712	80.3	5.3	13.0
Other districts	6106	84.3	2.88	
National	6818	84	3	0.00

PD-781-27 Factors contributing to time to sputum conversion among migrant populations treated for pulmonary tuberculosis in IOM, Kenya, 2010–2014

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Background: Globally, tuberculosis (TB) treatment success rate has remained relatively unchanged at about 86%. Untreated infectious TB cases continue to infect new cases and hence defeating the efforts towards ending the TB epidemic. On average one untreated infectious TB case will infect 15 people annually. 90–95% of cases on appropriate treatment will have negative sputum cultures by 3 months. Pre-immigration health assessment for USA, Canada, Australia, New Zealand, and UK includes active screening for Tuberculosis. The International Organization for Migration (IOM) performs pre-immigration health assessment for migrants to above countries, and ensures that those diagnosed with TB disease get appropriate TB treatment.

Intervention: Hopeful migrants who are referred for pre-immigration health assessment undergo TB screening which includes: history review, Physical examination, chest X-ray and sputum analysis where indicated. Those who meet the TB case definition are treated under Directly Observed Therapy (DOT) and monthly sputum smear and culture testing done and clinical reviews. Various patient characteristics were analyzed to find out what factors had significant contribution to time to sputum conversion and eventual treatment outcome.

Results: From 2010 to 2014, the IOM Clinic registered and treated 220 patients with PTB. Of these 28 were bacteriologically negative while the remaining 192 were bacteriologically confirmed with sputum smear or sputum culture positive. The treatment success rate was 94% (175 cured and 32 treatment completed), 6% had negative outcomes (4 died, 3 defaulted, 6 transferred out). The majority 166 (86%) sputum converted by month 1 of treatment, 20 (10%) by month 2, 5 (3%) by month 3, and 1 (1%) by month 5. Using survival analysis, baseline bacteriological load was found to be a significant factor influencing time in months to sputum conversion ($P = 0.0383$). Age, sex, nationality, migrant type, New or re-treatment, HIV and treatment duration were not statistically significant in determining time to sputum conversion.

Conclusion: Baseline bacteriological load was found to be a significant factor affecting time to sputum conversion. More data needs to be collected to reveal which other factors influence time to conversion, reducing continued transmission and thus better inform stakeholders in TB case management.

18. TB modelling, prevalence and surveillance

PD-782-27 Systematic review of mathematical models exploring the epidemiological impact of future TB vaccines

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Background: Mathematical models are essential tools for assessing the potential epidemiological impact of future tuberculosis vaccines to guide development of new candidates. No systematic review of this literature exists. We conducted a systematic review of mathematical models estimating the epidemiological impact of future human TB vaccines delivered to any age group when compared to no vaccination, other novel vaccine profiles or other TB control interventions.

Methods: PubMed, Embase and WHO Global Health Library were searched, and three-stage manual sifting conducted to identify studies meeting inclusion/exclusion criteria. Included articles were citation- and reference-tracked. An adapted study quality assessment tool was developed for scoring included articles. A protocol summary is registered on PROSPERO (reference:CRD42016033266).

Results: A total of 919 records, comprising 884 unique articles after removal of duplicates, were identified. Twenty-three articles were included in the review. The literature remains divided as to whether vaccines effective pre- or post-infection would provide greatest epidemiological impact. However, all-age or adolescent/adult targeted prevention of disease vaccines achieve greater and more rapid impact than neonatal vaccines. One-off mass campaigns alongside routine neonatal vaccination can have profound additional impact. Economic evaluations found TB vaccines overwhelmingly cost effective, particularly when targeted to adolescents/adults. The median study quality score was 20/28, and the quality assessment highlighted the importance of thorough reporting and conduct of comprehensive uncertainty and sensitivity analyses in future studies. It is hoped that this quality assessment tool will be of broad use in future systematic reviews assessing epidemiological models of other interventions and diseases.

Conclusions: Mathematical modelling has been used to understand how the epidemiological impact of future vaccines could be altered by vaccine characteristics, age targeting, and epidemiological setting. It has proved important for exploring the potential role of new vaccines for achieving the WHO 2050 goal of tuberculosis elimination. Given its critical importance for development priorities, modelling to understand the differences in impact when comparing pre- and post-

infection vaccines is urgently needed. Modelling should be integral to the development of future TB vaccines, informing rational decision making by cross-product bodies, academia, industry and policy makers for the development, investment and implementation of pipeline vaccines.

PD-783-27 The use of sub-national TB modelling to inform decision-making in South Africa

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Background and challenges to implementation: South Africa has one of the highest rates of tuberculosis (TB) in the world, and the disease is the leading cause of death. TB activities are driven primarily at the provincial level, making the availability of a tailored sub-national planning tool highly valued. As a proponent of the Global Plan to End TB, South Africa has been instrumental in establishing 90-90-90 TB targets which, if achieved, modelling suggests may have a significant impact on the TB epidemic. We describe the application of a TB transmission model at sub-national level and its use in estimating the impact of 90-90-90 targets and supporting decision-making at provincial level.

Intervention or response: 'TIME Impact' is an epidemiological transmission model nested in TIME, a set of TB modelling tools available for free download within the widely-used Spectrum software. The model uses TB programme performance indicators such as treatment success and linkage to care, and automatically incorporates UNAIDS estimates of HIV burden. With input from provincial TB experts and the South African National TB Programme, baseline models were calibrated to provincial TB case notifications for all nine provinces in the country. Two workshops were held with provincial TB managers to introduce the sub-national models and their applicability within the context of existing TB control activities.

Results and lessons learnt: The nine calibrated provincial models reflect the national epidemic to within 5% of 2014 case notification numbers. Provincial TB managers were enthusiastic about the potential of these models to inform their short- and medium-term planning, with a focus on 90-90-90 targets. During the workshops, each province provided input to refine the initial fits. Enthusiasm from policy makers requires management of expectations, as constraints remain with the in-country capacity to provide technical assistance, e.g. providing sub-provincial models for high-priority districts. Concerns were raised around sub-national data

quality and gaps e.g. case notifications and TB deaths through vital registrations.

Conclusions and key recommendations: Applying the TIME Impact model to the provincial level and running workshops was feasible, and may be a useful tool to focus attention on critical data gaps and inform provincial decision-making.

PD-784-27 TIME modelling to estimate the potential impact of case-finding activities in Ghana

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Background and challenges to implementation: In 2013, Ghana's TB prevalence survey showed that the burden is four times higher than previously thought (290 vs. 71 per 100 000). In mid-2015 Ghana began the implementation of their Global Fund to Fight AIDS, TB and Malaria (GFATM) grant under the New Funding Model. We worked closely with the National Tuberculosis Programme (NTP) to model the country's TB epidemiology in TIME based on the prevalence survey findings and estimated the potential impact of interventions from their National Strategic Plan (NSP).

Intervention or response: Engagement with the NTP and other stakeholders was done through team visits to Accra. We held discussions to collate and verify country data and performed a detailed review of the NSP. The country data and NSP were modelled using the TIME model to generate a projection of the TB epidemic, calibrating to notifications, number of suspects tested, prevalence, and WHO estimates of incidence and mortality. We then modelled the main NSP interventions that focussed on 90 high-priority districts to estimate the potential number of notifications and population-level impact on prevalence over the course of the GFATM grant and until 2025. We also investigated the impact of expanding activities to 113 districts and to full nationwide coverage (216 districts), accounting for procurement limitations of screening and diagnostic tools. Results were used to inform policy decisions around programme implementation and viability of the targets in the GFATM Performance Framework.

Results and lessons learnt: The modelling exercise showed that current coverage of NSP activities were unlikely to achieve Ghana's performance targets for notifications. Expansion of case finding activities should be considered when reprogramming the existing Global Fund grant. Modelling suggested that expansion of activities from current 90 to all 216 districts would lead to increased notifications (~22%) by 2017, but still fall short of the targets.

Conclusions and key recommendations: The TIME model assessed the feasibility of achieving the ambitious targets and highlighted additional operational challenges of the NSP. This informed the NTP and GFATM on what was attainable, leading to revising the scope of case

finding strategies and the application of reprogrammed funds.

PD-785-27 Estimating tuberculosis incidence from primary survey data: a mathematical modeling approach

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Background: There is a pressing need for improved estimation of the burden of tuberculosis (TB), in high-burden settings. Here we aimed to develop new quantitative methods based on primary TB survey data, and to demonstrate their application to the TB epidemic in India.

Methods: We developed a simple model of TB transmission dynamics, to capture the annual risk of TB infection (ARTI) and prevalence of smear-positive TB: quantities that are routinely estimated in prevalence surveys of TB infection. By determining key transmission parameters from this data, the model estimates implied TB incidence. As validation, we first applied the model to previous work on prevalence survey data from China, Korea and the Philippines. We then applied the model to estimate the incidence of TB in India, with prevalence survey data stratified by urban and rural settings to take account of the contrasting epidemics in these different settings.

Results: Model estimates for the number of secondary infections per smear-positive case show good agreement with independent estimates in previous work. Applied to India, the model suggests an annual incidence of smear-positive TB of 90 (95% C.I. 47.6–154) per 100 000 population. Results also cast light on contrasting factors in the epidemiology of urban and rural TB: while an urban TB case infects more individuals per year, a rural TB case remains infectious for appreciably longer, suggesting a need for interventions specific to these different settings.

Conclusions: Simple models of TB transmission, in conjunction with necessary data, can offer approaches for burden estimation that are complementary to those currently being used.

PD-787-27 Epidemiology of tuberculosis among persons born in the former Soviet Union living in the United States, 1993–2013

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Background: Global migration notably affects the epidemiology of tuberculosis (TB) in the United States (US). After the collapse of the Soviet system in 1991, immigration to the US from former Soviet Union (FSU) significantly increased. We describe the epidemiology and trends of culture-positive TB among persons born in

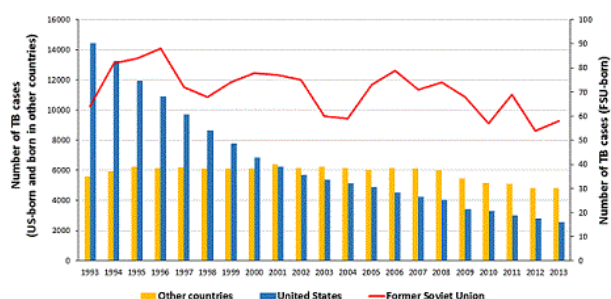
the FSU compared with cases born in the US and in other countries.

Methods: We analyzed data from all culture-positive TB cases reported in the US National TB Surveillance System, 1993–2013. Cases with missing data on country of birth or born as US citizens outside of the US were excluded from analysis. We used χ^2 tests to detect differences in proportions and assess trends.

Results: Of 264 444 culture-positive TB cases reported, 138 747 (52.5%) were US-born, 1484 (0.6%) were born in FSU, 123 121 (46.5%) were born in other countries. Among 1484 FSU-born persons, 52.2% were males (vs. 60.3% and 66.7% among US-born and born in other countries, respectively, $P < 0.0001$), 0.9% had positive HIV status (vs. 6.5% and 14.3%, $P < 0.0001$), 9.6% were previously diagnosed with TB (vs. 4.7% and 5.2%, $P = 0.003$), 6.8% had multidrug resistant TB (MDR-TB) (vs. 1.8% and 1.1%, $P < 0.0001$). The median age of FSU-born TB cases was 55 years and 42.3% were >65 years (vs. 19.4% and 27.2%, $P < 0.0001$). The annual number of FSU-born persons with TB has not significantly changed since 1993 compared to the number among US-born persons which has decreased more than 5 times during the same period ($P < 0.0001$). The proportion of FSU-born TB cases among all TB cases has increased from 0.3% in 1993 to 0.8% in 2013 ($P < 0.0001$).

Conclusions: Although the number of TB cases among US-born persons significantly decreased since 1993, the number of TB cases born in FSU and other countries did not change. FSU-born TB cases have higher proportion of relapse and MDR-TB compared to TB cases from other countries. TB in foreign-born populations remains a major challenge that delays progress toward TB elimination in the US.

Graph. Annual number of culture positive TB cases by place of birth. United States, 1993–2013



PD-788-27 Heterogeneity of distribution of tuberculosis in Sheka Zone, Ethiopia: health care-associated drivers and temporal trends

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Background: Although Ethiopia is among the 30 highest tuberculosis (TB) burden countries, the epidemiology of TB is not well described in geographically remote regions of the country.

Methods: We collected data on TB patients registered for treatment from 2010 to 2014 in Sheka Zone, Ethiopia to describe TB epidemiology and trends. Multivariate generalized linear regression was used to identify variables associated with TB incidence by year and *kebele* (the smallest administrative geographical subdivision in Ethiopia).

Results: We found significant spatial autocorrelation of TB incidence by *kebele* (Moran's $I = 0.3$, $P < 0.001$). Average TB incidence per *kebele* ranged from 0 to 453 per 100 000 per year and was significantly associated with average TB incidence across adjacent *kebeles*, TB incidence in the same *kebele* in the previous year and proximity to health facility. An increase in average TB incidence by 10 per 100 000 per year in adjacent *kebeles* or in a previous year predicted an increased TB incidence of 3 per 100 000 and 5.5 per 100 000 per year respectively. Availability of a health center was associated with an increase in TB incidence of 84.3 per 100 000.

Conclusions: TB incidence in rural Ethiopia is highly heterogeneous and shows significant spatial autocorrelation/ clustering. Both local transmission and access to health care are likely drivers of this pattern. Identification of local TB hotspots may assist in developing and optimising effective local strategies.

PD-789-27 Spatial and spatio-temporal risk clusters of occurrence in an endemic area of the São Paulo State, Brazil

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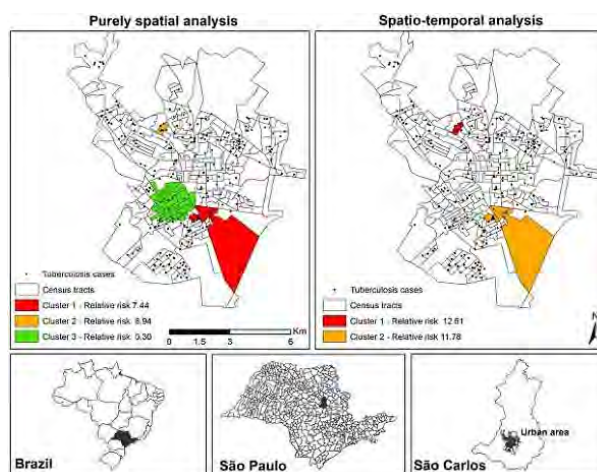
Background: Tuberculosis (TB) is an endemic issue in Brazil with an incidence rate of 36.1 cases per 100 000 inhabitants (2014). To reach the goal of TB elimination, it is relevant to identify areas and vulnerable population under risk to occurrence of TB. Study aimed to map the spatial and spatio temporal cluster under risk for the occurrence of TB cases.

Methods: Ecological study, whose studied population encompassed TB cases recorded in the Control System of Patients with TB between 2008 and 2013. The spatial distribution was performed through Terraview 4.2.2 and scan statistical analysis at the Satscan 9.4.2 (discrete Poisson model). It was considered the time precision in years and the population data were standardized by sex and average age of 42 years. The relative risk (RR) was calculated considering 95% of significance level.

Results: There were identified 315 TB cases with geocoding of 290 (92%). Three significant clusters were identified (Figure): the first ($P = 0.001$), consisting of three census tracts, population of 2035 people, 20 cases of TB, average rate of 160.2 cases per 100 000 inhabitants and RR 7.44; the second ($P = 0.005$), comprising one census tract, population of 1221 people, 11 cases of TB, average rate of 153.9 cases per 100 000 inhabitants and RR 6.94; the third ($P = 0.04$), protection, consisting of 29 census tracts, population of 19 025 inhabitants, 9 cases of TB, average rate of 7.4 cases per 100 000 inhabitants and RR 0.3. According the spatio temporal analysis two clusters were identified; the first ($P = 0.001$) in the period from 2010 to 2012, with the presence of one census tract, population of 1221 people, 10 cases of TB, average rate of 279.7 cases than 100 000 inhabitants and RR 12.6; the second ($P = 0.001$) in the period from 2011 to 2013, consists of three census tracts, population of 2035, 16 cases of TB, average rate of 256.3 cases per 100 000 inhabitants and RR 11.78.

Conclusions: The definition of clusters led to the identification of risk areas of TB cases, supporting the health planning for the elimination of TB.

Figure Spatial clusters of cases of tuberculosis



PD-790-27 Disease surveillance through mobile phones: geotagging the 'smart-phone' way

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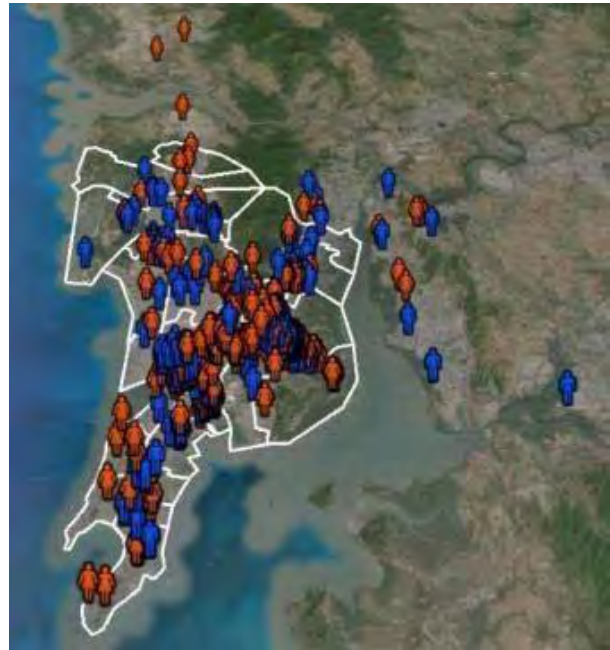
Background and challenges to implementation: Disease surveillance is crucial from the perspective of planning in the public health domain. Through the Private Provider Interface Agency (PPIA) the engagement of private providers is designed to improve TB diagnostic and treatment practices in the private sector in Mumbai. For effective surveillance and service delivery provision, PPIA listed and mapped private healthcare facilities, hospitals, clinics, laboratories, and chemists, and located homes of patients diagnosed as drug resistant (DR) TB. This was accomplished via geotagging through mobile phones.

Intervention or response: Field workers (FWs) used Global Positioning System (GPS) enabled mobile phones to geotag private healthcare facilities. FWs clicked images of healthcare facilities and kept the location tag switched on. Subsequently, photos were synced on the cloud based system Dropbox. Data entry operator at the back-office downloaded the images and geo-coordinate extracts using open source software. Geo coordinates were then added to a master excel file containing the details of private healthcare facilities. Geo coordinate files were uploaded on Google Maps software. For geotagging location of DR-TB patients, pin code of the house was used and was captured at the time of patient registration.

Results and lessons learnt: In Mumbai, 501 private healthcare facilities and 1388 DR-TB cases were geo-tagged. Clustering of DR-TB cases was seen in Kurla and Govandi areas of Mumbai. Cluster identification helped in prioritizing areas for private healthcare facilities engagement.

Conclusions and key recommendations: Geotagging healthcare facilities helps in spatial representation and is useful in disease surveillance. GPS enabled mobile phone is an easy, handy and cost effective way for geotagging location of healthcare facilities. This tool should be utilized in an intensive manner in the healthcare sector.

Figure Disease surveillance through mobile phones



PD-791-27 The Zimbabwe National Tuberculosis Prevalence Survey 2015: unexpected findings and implications for prevention and control

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Background: Zimbabwe completed its first national tuberculosis (TB) prevalence survey in July 2015. Results of the survey have very important implications for TB prevention and control in the country.

Methods: Using standard WHO guidance, the TB prevalence survey field work was carried out from January to December 2014. Data analysis and report compilation was completed in July 2015.

Results: The prevalence of TB in Zimbabwe was found to be 292 cases per 100 000 population. The TB case detection rate was increased from 42% to 72%. A total of 43 443 participants were invited for the survey and 33 694 (77.5%) participated. Of the 33 694 participants, 14,178 (42%) were males and the rest (58%) were females. All participants were 15 years of age and above. TB prevalence peaked within the age band 34–44 years and another peak was observed at the age above 65 years. Symptomatic screening detected 5820 participants as presumptive TB cases. Out of these, 5705 (98%) submitted sputum for smear examination and 206 (3.6%) were smear microscopy positive. Of the smear positives, 76 (37%) were culture positive. Out of these 76 culture positive 55 (72.4%) were mycobacterium

other than tuberculosis (MOTT). Among the 5499 smear negative participants, 998 (%) were culture positive and 909 (91.9%) of the culture positive were MOTTs. Symptoms alone were not specific for TB, 2797 participants had no symptoms but they had abnormal chest X-rays (CXR). 628 participants had a combination of symptoms and CXR abnormalities and among them, 63 confirmed TB cases were detected. Among male participants, 32.9% were smokers and 1.3% of female participants were smokers.

Conclusions: Urgent review of the current national TB targets and strategic interventions is imminent. Chest X-Ray and molecular tests need to be prioritized for active case finding of TB among priority risk groups. Smoking cessation among TB patients needs to be prioritized as well as research on the proportion of MOTT among smear positive clinical patients.

19. Intensified case finding

PD-792-27 Behind the scene and the stones: active TB case finding in a quarry population in Nigeria

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Background and challenges to implementation: In Ebonyi State, Nigeria, communities with the largest stone quarries have continuously reported very few cases of TB to the National TB Programme (NTP). We investigated the yield of active TB case finding in these quarry communities.

Intervention or response: A prospective implementation study was conducted by Annabelles Bogi Development Initiative (ABDI), Nigeria-a civil society organisation with funding from TB REACH. The intervention consisted of advocacy, communication and social mobilisation of the communities through community gatekeepers, and volunteers; household contact tracing of index TB patients, home visits, screening of TB-HIV patients, facility screening of out-patients and industrial site screening of quarry workers. Individuals presumed to have TB were referred to the nearest microscopy centres for investigation. Notified patients initiated treatment through the NTP.

Results and lessons learnt: A total of 5798 persons were screened over the 10 months intervention period. The number of persons with presumed TB found was 4520; and 3884 of which completed microscopy. Overall, 54 all forms of TB (46 smear-positive and 8 smear negative) were found. The number of TB cases notified increased from 4 before the intervention to 54 cases after the intervention, i.e., a 1150% increase (Figure). Also, contact tracing yielded 21 new cases, followed by home visits (17), facility-based screening (8), community

mobilization/mobile screening (6) and mobile camping (2). Major challenges faced were lack of trained laboratory personnel in some of the microscopy centres in some of the basic management units as well as poor accessibility to the communities. Also, industrial site screening of quarry workers yielded no cases.

Conclusions and key recommendations: We have demonstrated the potential role that can be played by a civil society organisation in enhancing community based active TB case finding in a rural resource-constrained industrial setting which may now be scaled-up.

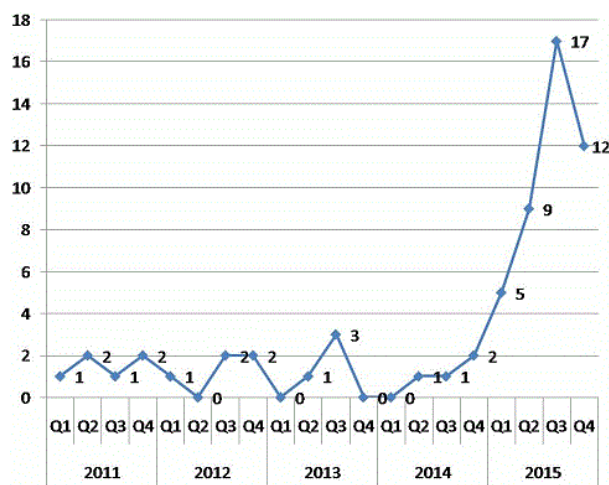


Figure1: Evaluation Population- Notified SS+/B+ Cases (2011-2015)

PD-793-27 Early TB detection among most at-risk population in Ukraine

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Background and challenges to implementation: As per World Health Organization assessment, about 25% of TB was not detected and registered in Ukraine, creating a reservoir of infection and contributing towards the TB epidemic. It may be assumed that non-detected cases are concentrated in MARPs who have limited access to health care services. To reach these population groups project on early TB detection was developed and launched in Ukraine.

Intervention or response: Project started in 2013 and covered clients of harm reduction programs (PWID, CSW and MSM) as well as special TB risk groups (ex-prisoners, Roma population, homeless). 79 field NGOs supported by Alliance implemented the project in all 27 oblasts of Ukraine. Activities included: screening questionnaire and referral to health care institutions for further examining those clients who were screening-positive. Patients with diagnosed TB are redirected to TB clinics to start treatment. Trainings on TB and advocacy issues for project managers and social workers were held to increase the capacity of NGOs to provide TB case

detection. All health care institutions in Ukraine were informed about the project launching. Roadmaps were developed in all oblasts for NGO clients.

Results and lessons learnt: The total number and rate of PWID with detected TB in Ukraine increased from 2.3% among all TB cases in 2012 to 7% in 2014 due to project implementation.

Conclusions and key recommendations: risk groups need to be paid special attention since they have limited access to health care services due to behavioral peculiarities, mentality and lack of registration. Patient roadmaps allow to extend and facilitate the access to TB diagnostics for representatives of risk groups. NGOs can be the link between the MARPs and health care system. WG on GF programs' sustainability recommended the activity on TB case detection among MARPs to be supported from domestic funding.

Table TB case detection results 2013–2015

	2013	2014	2015
Covered with screening	55549	38720	159513
Screening positive	12305	6123	17850
Examined in HC institutions	5698	5214	14699
TB detected	626 (11%)	510 (10%)	563 (4%)

PD-794-27 Empowering local NGOs to control the TB burden in the private sector

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Background and challenges to implementation: Private Provider Interface Agency (PPIA) is engaged by Mumbai government for working with the private sector for universal access to TB care. PPIA is engaged with two local NGOs - Alert India and Maharashtra Janavikas Kendra for patient management and case notifications and ensure early diagnosis and treatment adherence in private sector.

Intervention or response: For private sector TB patient management, these NGO health workers are involved in providing the engaged private providers free diagnostic and treatment vouchers. The NGOs were trained in managing database process of the patients from TB notification to sputum sample collection, transportation till the laboratory diagnosis within 24 to 48 hours for early initiation of treatment. Laboratories and chemists providing services through vouchers are reimbursed by the NGOs. 80% of the reimbursements to laboratories and chemists is completed by the NGOs within 7 days of receiving the invoices and vouchers. Patients are also monitored through calls, SMSs and visits for treatment adherence and completion by the health workers of NGOs.

Results and lessons learnt: 43 314 presumptive TB cases have been recorded with 16 839 TB patients with 4,053 patients having successfully completed treatment. More than 1200 patients are detected with TB every month under the PPIA networked doctors. Apart from this, 14

230 CBNAAT test have been conducted and managed by the NGOs. USD 600 000 have been reimbursed by these NGOs. This initiative of involvement of the local NGOs has empowered them in improved management of tuberculosis patients in private sector and ensured data recording and notifications. This is an example of community involvement of the local NGOs to streamline quality tuberculosis case management in private sector in Mumbai having highest burden of TB cases.

Conclusions and key recommendations: NGOs now have the capacity to handle process oriented programs with use of technology and with adequate training track patient movement and treatment adherence for contagious diseases like TB and can be replicated for control of other diseases.

PD-795-27 Role of the community in counselling clients in accessing health services and retention on tuberculosis treatment

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Introduction: Tuberculosis (TB) remains one of the world's deadliest communicable diseases. In a poor and under-developed country such as Nepal, TB is a major public health problem. About 45% of the total population is infected with TB disease of which 60 percent are adult. Every year, 45 000 people develop active TB; of these 20 580 have infectious pulmonary disease. These 20 000 people are able to spread the disease to others. Treatment by DOTS has reduced the number of deaths; however 5000–7000 people in Nepal are still dying each year by TB. The overall objective of the study was to explore the situation of people living in remote and hard-to-reach communities in accessing health services related to tuberculosis.

Method: The descriptive qualitative study was carried out in six clusters of purposively selected districts of Nepal. The sample districts were selected in such a way that they were representing the districts of all five development region. The study was carried out by using Focus Group Discussions (FGD). FGD was conducted involving three types of people representing key affected population, community service providers and related focal person of TB of study districts. The study was focused to assess the situation of people in accessing health services related to TB in the study district and three selected prisons. The collected data were systematically and thoroughly analyzed and interpreted under the basis of stated objectives and findings.

Results: The study explored that the services of TB in remote and mountainous districts are not sufficient and effective. Access in services and retention in treatment is a challenge resulting low case findings and high drop out rates. Stigma and discrimination among TB patients is high in the community and family of TB patients. Counseling services at the health facility is not available and community engagement is quite low.

Conclusions: Community system to increase access of underprivileged and deprived communities in services and treatment of TB and to sustain the activities of TB should be strengthened.

However, the role of community in counseling clients to access in services, retaining in treatment, mitigating stigma and discrimination is crucial.

PD-796-27 Community outreach as a model for increasing TB case finding: lessons learnt from six high-burden states in Nigeria in 2014

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Background: Nigeria ranks high among the 30 high TB burden countries globally. TB Case Detection Rate (CDR) for 2014 is 15%. In a bid to address the low CDR, community TB outreaches was conducted in six high TB burden states (Kaduna, Kano, Rivers, Anambra, Lagos and Imo) in September 2014. This study aim at demonstrating the lessons learnt in the 6 states in the use of community outreaches as a model for increasing TB case findings.

Methods: This cross-sectional study was carried out in six states which were purposively selected based on some set criteria which include, but not limited to: high TB burden and high urban slum population. An advocacy/assessment visits was conducted to the states to obtain the buy-in of the community-actors. Community-workers and the Health staff were trained. The outreaches was conducted in one week in an average of one community per state, two sputum specimen from presumptive cases were tested using the front-loading system and those diagnosed with TB treated appropriately.

Results: 2674 presumptive TB cases were identified during the outreaches (Anambra 430; Imo, 343; Kaduna 545; Kano 456; Lagos 450; and Rivers 450). States with higher HIV prevalence has a higher proportion of TB cases detected among presumptive TB cases. 81 smear positive TB cases were diagnosed in the six states in one week, almost all are adult and were not accessing any prior TB services. HCT and Malaria rapid testing was offered to all the presumptive and confirmed TB cases in Imo state.

Conclusions: Engagement of the community in the planning process lead to mobilization of additional community-resources and facilitated huge turnout of presumptive TB cases. The engagement of the HIV and Malaria programme in the planning stage of the outreach in Imo state facilitated the delivery of an integrated TB, HIV & Malaria services.

Community outreaches should be considered as one of the way forward in addressing challenges of low CDR. TB programme while conducting outreaches should engage all stakeholders including HIV programme to enhance access to additional resources/services. GeneXpert technology, diagnosis of EPTB and childhood-TB should be incorporated into TB outreaches to address missing cases during outreaches

PD-797-27 Gaining momentum through effective partnership in tuberculosis control programme, Bangladesh

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Background and challenges to implementation: Bangladesh is a high TB burden country in the world. National TB control programme (NTP) adopted the DOTS strategy since 1994 and expanded the services to cover the country in collaboration with Non Government Organization (NGO) partners. NTP and its NGO partners continued the momentum of this control effort with limited resources.

Intervention or response: The National TB Control Programme under the Directorate General of Health Services (DGHS) has been implementing TB control strategies in collaboration with the NGOs. Specific areas are assigned to NGOs through existing and/or new MoU for scaling up the programme implementation. BRAC signed an MoU with the Government in 1994 for rural areas and another in 2001 for urban areas. Gradually, the partnership has been built up through MoUs with different groups of NGOs who are supporting the government health system by expanding availability of DOTS and other critical TB control activities. The partnership approach ensures efficient use of limited resources, avoidance of overlapping, high cure rate and quality assured sputum microscopy.

Results and lessons learnt: Countrywide programme coverage has been established. The case notification rate of all forms of TB cases in 2014 was 122/100 000 population which was 59/100 000 population in 2001. Treatment success rate of the country is 94% in 2014 which has got a sustainable level.

Conclusions and key recommendations: Partnerships provide the programme a strong technical base including sharing and cross learning. The new and emerging areas need to be faced with the same effort and it should also be in a sustainable way during development of strategy.

PD-798-27 Household intensified case finding in a high TB-HIV burden setting: who do you find? A TB REACH experience in Swaziland

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Background: Intensified case finding (ICF) in communities increases TB-HIV case detection. Swaziland would benefit from innovative, efficient programs to increase TB case notification, currently at 60%. Few ICF programs have explored their impact on both TB and HIV epidemics. With TB REACH funding, Baylor College of Medicine Children's Foundation-Swaziland (BCMCF-SD) implemented a community-based ICF program to increase TB case detection among HIV-affected households.

Intervention: BCMCF-SD screened household contacts of index cases (ICs) initiating TB treatment in 7 health facilities. Those screened TB positive on report were referred to a health facility for sputum submission. Home visits were conducted to complete TB screening and sputum collection for contacts with presumptive TB who didn't reach a health facility. Bacteriologically-confirmed contacts were referred to start TB treatment. Symptomatic contacts with negative sputums were referred for further evaluation and treatment accordingly. We describe the population reached through household ICF from May 2013–November 2015, according to age, gender, self-reported HIV-status, and number of additional TB cases.

Results: 3255 ICs were linked to 858 households yielding 5235 contacts. 49% (2588/5235) of contacts provided sputum and 88% (2275/2588) did so during the home visit, resulting in diagnosis of 2% (37/2275) additional bacteriologically confirmed TB cases. Although representative of Swazi demography, our sample's sputum positivity mainly captures females (65%) and 20–50 year old individuals (69%) (Table). HIV-positivity was disclosed by 9% (462/5235) of contacts while 55% (2899/5235) reported an unknown HIV-status. Males and adolescents (10–19 years) were more likely to report an HIV unknown status ($P < 0.01$).

Conclusions: Although effective at finding additional TB cases, household-based ICF strategies have limited potential to identify bacteriologically confirmed cases among children, adolescents and elders in this setting. Our model of household contact tracing provides an ideal opportunity to reach a representative population of Swaziland and to extend TB-HIV services to hard-to-reach populations, thereby reducing the TB burden.

Table Population distribution and confirmed TB cases

Characteristics	DHS 2007 (N=22,612)	BCMCF-SD home visits profile (N=5,235)	BCMCF-SD sputum positive (N=37)
<20 years	56%	56%	25%
20-50 years	33%	33%	69%
>50 years	11%	11%	6%
Female/male	55% / 46%	56% / 44%	65% / 35%

PD-799-27 Mobilizing community health volunteers can contribute to early case finding in Kathmandu Valley, Nepal

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Background and challenges to implementation: TB is one of the most widespread infectious disease in Nepal, and poses a serious threat to the health and development of the people of this country. About 60% of adults and 45% of the general population have been infected every year. It is not surprising that the highest rates of infection have been found in the most densely populated areas, such as Kathmandu valley and other major urban areas.

Intervention or response: This cross sectional study was done in Kathmandu valley focusing on garbage collectors, people living with TB symptoms, visits to private pharmacies, street children's and contacts of Tuberculosis Patients. The trained community health workers and volunteers conducted intensive community mobilization activities, performing door-to-door visits to refer the people living with TB symptoms found in community to near by microscopy centers or mobile microscopic camps for the sputum examination. Two sputum samples including one early morning and 1 spot specimen were collected in same day.

Results and lessons learnt: Among total (112 341) person screened, 24 065 (21%) were identify with TB sign and symptoms. 83% (20 123) people living with TB symptoms identified in the community and private pharmacies visited for the sputum examination. Among total examine 220 people were diagnosed as Sputum Smear Positive (SS+). Nearly two third of diagnosed cases were male and their mean age was 37. The intensive community engagement activities and door-to-door visits improve the health seeking behavior of the target groups. Among total diagnosed cases 212 (96%) cases enrolled their treatment from the near by DOTS centers. This intervention contributes 12% (220/1859) of the additional TB case finding in the Kathmandu valley.

Conclusions and key recommendations: The Public-Private Mix (PPM) activity in the community supports to maintain the motivation level of key stakeholders. Continue and quality mobilization of key stakeholders can contribute to increase additional case finding from the hard to reach population. Endorsing the evidence-based activity in regular programme of NTP could be the best way to sustain and reach the unreached population and maintain the cost effectiveness of community-based activity.

PD-800-27 Improving TB case finding through organized and trained community volunteers in San Juan City, Philippines

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Background and challenges: TB case finding in San Juan City (population: 123 013) is largely passive. Health facility medical teams usually wait for presumptive TB patients to seek consult on their own accord. However, many patients do not go to the health center because they do not know they have TB, and are unaware of the signs and symptoms of TB, and the services available at the health center. If they do know they have TB, they are ashamed to let other people know about it. No TB education and information campaign was conducted in the community except during patient's consultation at the health center. Community volunteers were unorganized and had no referrals from the community. Recording and reporting were mostly based on the forms provided by the National Tuberculosis Control Program, which at the time did not report on community referrals.

Intervention: In July 2014, USAID/Philippines organized and trained community volunteers, known as TB Task Force, from all *barangays* (villages). Organizing the TB Task Force involved 1) advocacy to ensure barangay government support, 2) interpersonal communication and counseling (IPCC) training of community volunteers and barangay leaders to ensure they understand the work of a TB Task Force member, 3) development of a recording and reporting system for the use of community volunteers, 4) establishment of a referral system between community volunteers and health centers, and 5) target setting right after training to define outputs and expectations.

Results and lesson learnt: The community volunteers conducted TB education through one-on-one sessions, small group discussions or community assemblies. This increased TB awareness in the entire city, which led to increased referrals. Two months after the volunteers' training, their referrals rose from zero to 36% (30/84), and to more than half the cases registered (66% [46/70]) the following quarter. Total contribution of the TB Task Force after a year was 32% (105/330).

Conclusion: With the support of the local government, organized community volunteers adequately trained on IPCC and armed with appropriate recording and reporting forms contribute significantly to community education and TB case finding.

PD-801-27 Experiences from conducting TB outreach campaigns in Water Front slums of Port Harcourt Local Government Area, Rivers state, Nigeria

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Background and challenges to implementation: The Global TB report 2015 put the current TB case detection rate for Nigeria at 15% after the results of the national TB prevalence survey conducted in 2012 which also revealed that most of the undetected TB cases in the community had obvious signs and symptoms. The National TB Control Programme (NTBLCP) responded to the challenge by conducting active TB case finding among slum populations in six states of the country. This paper reports on the response efforts by NTBLCP and supported by WHO country office and the lessons learned will inform a more inclusive engagement of affected communities in similar interventions in future.

Intervention or response: Advocacy and sensitization of community leaders in waterfront slums of Akokwa, Afikpo, Egede, Nanka, Okwelle and Timber of Port Harcourt Local Government Area (PHALGA) followed by orientation of community volunteers and GHWs, mobilization of the communities and conduct of house to house active TB case search using a structured checklist of questions on signs and symptoms of TB from 10–20 December 2015. Every identified presumptive TB case was requested to produce spot sputum sample and second sample collected 1 hour later. The sputum specimens collected were transported to 3 designated laboratories and were examined by AFB microscopy or GeneXpert MTB/RIF test.

Results and lessons learnt: A total of 3096 households were enumerated with 3944 household members screened clinically for signs and symptoms of TB; 801 (20%) presumptive TB cases were identified and sputum collected and transported to laboratory for examination. The results showed that 14 (2%) were bacteriologically positive by either AFB microscopy and/or GeneXpert MTB/RIF test. There was no Rifampicin resistance. Poor sputum specimen handling and transportation, inadequate human resources, poor documentation and reporting constituted some challenges experienced during the exercise.

Conclusions and key recommendations: Although the active TB case search in waterfront slums of PHALGA yielded unexpected low cases of TB, the lessons of inadequate laboratory personnel, poor handling and transportation of sputum samples, poor documentation and insecurity underpins importance of adequate design, assessment and engagement of communities at risk for active TB case finding.

ABSTRACT PRESENTATIONS FRIDAY 28 OCTOBER 2016

e-POSTER SESSIONS

06. Community-based approaches for TB

EP-148-28 TB detection rates through community mobilization vs. household contact investigation in rural South Sudan

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Background and challenges to implementation: TB remains a global public health problem, despite control efforts including early case detection and treatment. In 1991, the WHO increased the case detection rate to 70%. South Sudan's case notification rate is 48%. Contact Investigation (CI) was piloted in Yei, Morobo, and Lainya Counties in July 2015 as a strategy to systematize active case finding.

Intervention or response: Two approaches for improving case detection were evaluated: 1) community TB mobilizers passed TB health education messages at community gatherings, schools, and markets, and conducted TB screening and presumptive TB case referral to health facilities for diagnosis. 2) TB community mobilizers trained in CI by the Challenge TB (CTB) team were given screening and referral forms. Newly diagnosed smear positive index TB patients were identified from TB Management Unit (TBMU) treatment registers and assigned to TB community mobilizers for contact tracing. TB community mobilizers contacted the TB index cases, and together with CTB visited index case households. The contact investigation screening form was used to record observations on the number of contacts living with the index TB patient, and signs and symptom for each household contacts. Presumptive TB cases were referred to a health facility for smear microscopy and further investigation.

Results and lessons learnt: Between July and September 2014, community mobilizers reached 10 740 people with TB health education messages. 3.0% (325/10,740) presumptive TB cases were identified and referred for laboratory investigation, with 1.5% (5/325) bacteriologically confirmed TB cases. Using the CI initiative, 892 bacteriologically confirmed index cases were registered, and 107 index case households were visited. Among the contacts screened, 21.3% (182/853) presumptive TB

cases were identified, of which 15.4% (28/182) were bacteriologically confirmed.

Conclusions and key recommendations: Using CI for case finding can yield 10 times more cases than community awareness campaigns. Tracing contacts of TB index cases is a feasible and effective method of increasing case finding, especially in poor settings where household contacts are high. CI training for community mobilizers in resource limited settings can have a significant impact on case finding.

EP-149-28 Notification of TB-HIV co-infected cases through a community-based approach

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Background and challenges to implementation: India has world's second highest annual estimate of 110 000 TB-HIV co-infected cases. Notification rate is around 40% (44 171), and it is conducted by intensified case finding (ICF) on TB and HIV service delivery sites followed by cross-referrals. Additional strategies are required to improve notification of TB-HIV cases. The NGO consortium led by World Vision India (WV India) contributed to improved notification rate of TB-HIV co-infected cases and utilization of collaborative TB-HIV services through community TB-HIV collaborative programs.

Intervention or response: During the Global Fund supported TB Project (Axshya) implementation in April 2013–September 2015, WV India with 6 partners established linkages with 65 district networks of people living with HIV (PLHIV) and 450 Targeted Intervention (TI) HIV projects in 74 districts of 8 states. Through using specific training modules, 2203 PLHIV and 398 Program Managers at the TI projects were sensitized on TB. They were assisted in developing and implementing their organizational TB action plans including creating case-wise line-lists of the referrals to TB services. These activities enabled PLHIV and HIV high risk groups to gain knowledge on TB, reduce stigma, improve self-screening of TB symptoms and better utilize the TB-HIV services.

Results and lessons learnt: Between April 2013 to September 2015 the PLHIV networks identified 1333 presumptive TB cases through community level TB education and ICF, 1276 of them were tested in local RNTCP-affiliated laboratories, with 114 found to be sputum smear positive pulmonary TB (positivity rate was 9%) while 111 of those received treatment. They were also initiated ART and CPT. The HIV-TI projects referred 950 presumptive TB cases from the high risk groups (FSWs, IDUs, migrants, MSM/TG and truck drivers), 874 of them were tested, 51 were confirmed as sputum smear positive pulmonary TB (positivity rate was 6%) and all those received TB treatment.

Conclusions and key recommendations: The NGO-consortium led by WV India demonstrated critical

importance of community-based TB-HIV collaborative programs for case detection, notification of TB-HIV co-infected cases and utilization of integrated TB-HIV services.

EP-150-28 When ex-TB patients start looking for other patients: results after 28 months in the South-Kivu province of DRC

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Background and challenges to implementation: An adequate response to chronic under-detection of TB cannot rely on fragile health systems overwhelmed by current activities. In order to respond to the need for additional human resources required for implementing active case-finding activities at a large scale, the National TB Program of the South-Kivu province in the Democratic Republic of the Congo (population of 6 million) has initiated an innovative collaboration with an organization of ex-TB patients. The rationale for involving ex-TB patients is to facilitate access to remote areas that the health system traditionally does not reach by involving people familiar with both the disease, its symptoms, and the communities to reach.

Intervention or response: Supported by TB REACH and CHALLENGE TB, ex-TB patients have been trained to perform door-to-door screening to identify patients with a cough lasting for more than 15 days, and to refer those individuals to the health facilities for a bacteriological investigation of sputum samples. These screeners provide monthly reports, which are validated by the health structure that ensures the medical follow-up of the patients as per national guidelines.

Results and lessons learnt: During the first 28 months of this collaboration, the organisation and the NTP performed 476 days of training and supervision in the 100 TB centers of the province. During this period, an average of 330 ex-TB patients reported screening activities each month. Altogether, they screened 683 088 individuals, among whom 10% (70 222) presented a cough for more than 15 days. 61% of these attended to the closest health facility for smear microscopy, and 8.3% of those tested were diagnosed with a smear positive pulmonary TB. The positivity rate remained relatively stable throughout those 28 months, although differences by regions were observed.

Conclusions and key recommendations: During a 28 months period, over 10% of the South-Kivu population has been screened for TB thanks to the implication of ex-TB patients. Incidence of bacteriologically confirmed pulmonary TB was 526/100 000, a figure about 6 fold higher than usually reported by the NTP when perform-

ing passive case finding of TB. This experience and the high figures reported tend to show the utility of this innovative collaboration.

EP-151-28 Redefining the scope of civil society for tuberculosis control by 2035: a unique initiative by The Union

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Background and challenges to implementation: TB remains one of India's greatest public health challenges despite the availability of effective therapies and largely successful national TB control programme. It has the highest burden of TB globally, with over 1.5 million new cases and 300 000 TB related deaths reported every year, and more than 73 000 patients estimated to suffer from drug resistant TB. Often, they live in difficult-to-reach areas, unable to access available diagnostic, treatment, and social support services, suffering and dying alone.

Intervention or response: Project Axshya is a civil society initiative and is being implemented by The Union in 300 districts across 21 states of India. The objective of the project is to support India's Revised National TB Control Programme to expand its reach, visibility and effectiveness by engaging community based providers to improve TB services, especially for women and children, marginalised, vulnerable and TB-HIV co-infected population.

Results and lessons learnt: The Project has created a network of 1200 NGOs and 20 000 community volunteers and has trained 25 331 unqualified healthcare providers who identify and refer TB symptomatics amongst the people who approach them for services. The TB patients and community is being empowered through 300 District TB Forums and working as a partnership between health system and community. Every month Axshya reaches out to 300 000 households creating awareness on TB and identifying and referring TB symptomatics. Active involvement of the community has resulted in identification and sputum examination of 692 219 TB symptomatics primarily from the marginalised and vulnerable populations during the period April 2013– September 2015. Of these nearly 547 892 (79%) symptomatics had their sputum collected and transported to the diagnostic centres saving cost and time delay. 58 279 TB patients have been diagnosed, treated and cured through DOTS.

Conclusions and key recommendations: The success of the community driven project led by Civil Society Organization has really shown a way to increase the access to quality TB care and services to the hard to reach areas; thereby minimizing delay in diagnosis and cutting the chain of transmission and to achieve the global targets. This model can be adopted by other countries.

EP-152-28 Educlowns and tuberculosis: community theatre, gender and TB awareness in rural areas of Tamil Nadu

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Background: India has one of the highest occurrences of tuberculosis (TB) and yet the disease is still highly stigmatized. A 2008 study found that nearly three times as many men were diagnosed with TB in Revised National Tuberculosis Control Programme Centres.¹ Despite this, women carry the highest burden of this stigmatization as it can greatly affect their marriage prospects.^{1,2}

Methodology: Between August 2014 and November 2015, Blossom Trust held seven Educlowns performances in four blocks of Virudhunagar, aimed at the general public. Performances took place in the evening when most people had finished work. An Educlowns performance averaged 400–500 audience members in villages and thirty minutes was designated for questions after the performance.

Results: The eight performers took questions from 50 people and identified 4 or 5 symptomatic patients per performance. While audiences were usually equally split between men and women, women were more likely to ask questions, about TB and other issues like HIV, cancer and sexually transmitted diseases. This suggests that the impersonal nature of the interactions allowed women to come forward and learn without feeling the stigmatization they may feel whilst talking with medical professionals. While previously impact was not efficiently measured, from 2016, performances will include time for surveys that will gauge the audience's level of awareness of TB before and after which will allow valuable analysis of the programme's effectiveness. Due to the irregular work hours in urban settings and the increased mobility and activity of the population, performances in towns have fewer audience members who will watch the entire performance. Thus performances could be tailored to the setting, by being shorter and more information rich.

Conclusions: The simple performances and anonymising costumes of Educlowns can be used to inform the public about high stigma issues from women's rights to preventing TB and HIV/AIDS. The programme only requires a few volunteers and costumes to be replicated in numerous contexts.

Figure Image of Educlowns



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EP-153-28 The 'TB missed call' initiative in the State of Punjab under Digital India

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Background and challenges to implementation: Leadership of India has the vision of Digital India. Digital services are viewed as a game changer in public health communication. Aiming to enhance access to information and services under Tuberculosis control, TB Missed Call initiative, a helpline with a toll free number 1-800-11-6666 was launched to provide information related to TB symptoms, treatment services available, and address and contact details of the nearest treatment facility in state of Punjab. An appraisal of the efforts made under TB Missed Call initiative can identify the requirements for further scaling up, modification or continuation of effort

Intervention or response: Information regarding Advocacy, Communication, Social mobilization (ACSM) activities undertaken during June 201–February 2016 under TB Missed Call initiative was collected and their appraisal was made.

Results and lessons learnt: Health care workers, public and patients were given awareness through meetings, pamphlets, charts, hoardings, news papers, radio/TV and putting up of stamps on OPD slips/RNTCP Documents. A total of 3376 calls were received. Under TB Missed Call initiative, of 1027 reasons for calling, general enquiry was most often the reason for the call with 404, address of Microscopy center for 295 calls, symptoms of TB for 160, need of help from DTOs for 50 calls. 118 of patients already availing TB services had

approached through TB Missed Call initiative. Source of information regarding TB Missed Call initiative by the caller was obtained through Posters/stickers in 51.7%, Newspapers in 34.3% and Health workers in 5.8% The total contribution about source of information was in less than 8% from Radio, Cinema, Television, Hoardings/Wall paintings or word of mouth.

Conclusions and key recommendations: Punjab state of India has population of 29.9 million and has 30.6 million telephone connections. Missed call campaign can be important ACSM activity for TB control. Print material/Media like posters/stickers and newspapers are better for noting toll free number as compared to audiovisual measures

EP-154-28 Promoting proper diagnosis and treatment of tuberculosis among employees through the workplace TB programme in the City of Calamba, Philippines

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Background and challenges to implementation: The City of Calamba has six industrial zones within its boundary. Despite the existence of an administrative order from the Department of Labor and Employment (DOLE), companies remained unaware of the TB-in-the-workplace policy. During pre-employment and annual medical examination, companies would often encounter applicants and employees with positive chest X-ray findings who were not referred to DOTS facilities for proper diagnosis and treatment. The city has only engaged one private company prior to 2013.

Interventions or response: In 2013, USAID/Philippines supported the engagement of 21 workplaces in two industrial zones in the city. The workplace TB program aimed to ensure that employees were informed about tuberculosis, TB presumptive employees were referred to the city DOTS facilities for proper diagnosis and treatment, and treatment of employees was supported by a treatment partner from the company.

The engagement of the workplaces involved advocacy meetings to orient the companies on the DOLE policy, program management training to assist them in installing the workplace TB program through a company policy, and TB educators training to capacitate selected employees to provide peer education.

The city legislative council passed an ordinance in 2015 to support and encourage workplaces to implement the workplace TB program. Additionally, the City Health Office (CHO) engaged 38 additional workplaces in two industrial zones.

Results and lessons learned: Implementation of TB control program in the workplace expanded employees' access to appropriate TB diagnosis and care. From zero contribution, the initial 21 engaged workplaces contrib-

uted 2% of notified TB cases in the city (30/1390) in 2014 and 3% (38/1248) in 2015.

Conclusion and key recommendation: Engaging companies in TB control ensured that employees received appropriate diagnosis and treatment for TB. The commitment of the local government unit to implementing the program is critical in monitoring and supervising the workplaces. Companies are willing to be involved once they have proper information on TB-DOTS and how it will benefit their employees and the company.

EP-155-28 Selection and engagement of civil society organizations in tuberculosis control: best practices from Amref Health Africa's Global Fund Tuberculosis Project

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Background: Engagement of communities and civil society organizations (CSOs) is one of the key pillars and components of ending the Tuberculosis (TB) epidemic by 2035. Amref Health Africa in Kenya has rich experience in TB control and has been implementing community TB activities through grass root CSOs on behalf of Kenya, under the non-state actors as one of the Principal Recipients (PR) for Global Fund TB Grants. Appointing SRs was previously done by the country's coordinating mechanism (CCM) and was based on subjective assessments of their track record.

Challenges to implementation: With devolution of health care services in Kenya, some counties expressed preference to work with a single sub recipient for TB work. Furthermore, limited/lack of local presence of SRs affected coordination, efficiency and effectiveness in implementation.

Intervention or response: An expression of interest for applications to be considered for sub-granting by the PR was advertised. Kenya Coordinating Mechanism (KCM) through Tuberculosis Inter-agency Coordinating Committee (TB ICC) constituted a Technical Review Committee (TRC) from different stakeholders. The TRC agreed upon selection criteria was carried out in three phases which included: Preliminary Review, Technical Review and Capacity assessment. Each Application was reviewed by three independent reviewers and average percent score was awarded.

Results and lessons learnt: 125 organizations responded to a public call for expressions of interest. 35.2% (44) of the organizations did not comply with application guidelines and were eliminated at the preliminary review phase. 63% (43) of the organizations that met technical requirements qualified for capacity assessment; out of which 67% (29) of the organizations qualified for sub granting by Amref Health Africa in Kenya. Grass root Civil Society Organizations (CSOs) and the communities they work in are key players in the delivery of health

services, as they have unique advantages in advocacy, demand creation and linkage of communities to services geared towards TB control.

Conclusions and key recommendations: A transparent, inclusive and fair SR selection and engagement process resulted in PRs and SRs emerging with a better understanding of each other's roles and capacities and better identification of organizations best suited to implement the grant.

EP-157-28 Analysing the impact of the context in which disease control programmes are embedded: a situational assessment of tuberculosis in Myanmar

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Background: There are numerous challenges in planning and implementing effective disease control programmes in Myanmar, which is undergoing a political and economic transformation whilst experiencing massive inflows of external funding. In light of the dearth of published literature on tuberculosis (TB) control in Myanmar, and the limited examples globally of broad situational assessments analysing the wider context in which TB control systems are embedded, we conducted a situational assessment of TB in Myanmar.

Methods: Between November 2013 and August 2015, we conducted a mixed methods analysis, including key informant interviews, participant observations and linked literature reviews, of how TB control strategies in Myanmar are influenced by the broader political, economic, epidemiological and health systems context using the SYSRA conceptual and analytical framework.

Results: The substantial influx of donor funding, in the order of one billion dollars over a five-year period, may be too rapid for the country's infrastructure to effectively utilise. Funding of numerous non-governmental organisations may result in the formation of a parallel service delivery system and measures are being undertaken to increase integration with the public health system. Our literature review identified very limited evidence to inform resource allocation decisions. TB control strategies thus far have tended to favour medical or technological approaches rather than infrastructure development, and appear to be driven more by perceived urgency to 'do something' rather informed by evidence of cost-effectiveness and sustainable long-term impact. Progress has been made towards ambitious targets for scaling up treatment of drug-resistant TB, although there are concerns about ensuring quality of care. We also find that there are substantial disparities in health and funding allocation between regions and ethnic groups,

which are related to the political context and health system infrastructure.

Conclusions: Myanmar presents a unique example of disease control programme planning and implementation during a period of rapid political and economic change and massive inflows of external funding. Success of the TB control programme, and of wider health sector reform, depends on whether political commitment and allocation of the substantial funding available are focused on cost-effective strategies that address rather than exacerbate health disparities.

07. TB transmission dynamics

EP-158-28 Transmission of *Mycobacterium tuberculosis* among children and adolescents in schools and congregate settings: systematic literature review and meta-analysis

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Background: Children, especially those aged < 5 years, and adolescents are vulnerable groups at higher risk of progression to active TB disease when infected. Management of childhood TB outbreaks is crucial to achieve TB elimination, as children with latent *Mycobacterium tuberculosis* infection (LTBI) could act as a reservoir for future TB cases.

Methods: We searched the electronic databases MEDLINE-CINHAL-EMBASE up to April 2015 to identify primary studies reporting on TB outbreaks where a teacher/child-caregiver, relative or student was diagnosed with TB, and children or adolescents aged 2–18 years in a school/childcare setting (including kindergarten, pre-school playgroups, day nurseries, day-care centres) and other congregate settings attended by children and adolescents, were exposed.

Results: Out of 9707 citations 68 studies, published mostly in low TB burden countries from 1950 to 2014 and describing 88 outbreaks, were selected. Outbreaks mainly occurred in school settings (74, 84.1%), where 46,536 children, mostly aged 5–15 years, were exposed to other students (50, 56.8%) and, less frequently, to teachers/caregivers (31, 35.3%) or bus drivers (8, 9.1%). Among 35 789 screened children (76.9% of those exposed), 5110 (14.3%) LTBI and 823 (2.3%) active TB cases were diagnosed. Pooled proportions of TB disease and LTBI among exposed individuals were 2.9% (95%CI 2.1–3.8; I^2 96.0%) and 13.7% (95%CI 10.7–17.2; I^2 98.9%), respectively, in 83 contact investigations attributable to a single index case. TB disease rates were higher: 1. following exposure to an index case with cavitary lesions (pooled proportions 2.2% (95%CI 1.4–3.3; I^2 94.9%) vs. 1.3% (95%CI 0.4–2.6; I^2 94.5%) if

absence of cavitary lesions); 2. following exposure to index cases aged ≤ 16 years (3.0% (95%CI 1.6–4.9; I^2 94.5%) vs. 1.3% (95%CI 0.8–1.9; I^2 92.2%) if older); 3. and in exposed individuals aged ≤ 6 years (7.3% (95%CI 3.7–12.1; I^2 83.4%), vs. 2.5% (95%CI 1.6–3.7; I^2 96.6%) if older).

Conclusions: The overall risk of TB disease in school settings seems higher than in household settings, especially when younger children were exposed. The relevant methodological heterogeneity may hinder the inference of the current findings. Public health interventions should be implemented to reduce the risk of LTBI and TB disease transmission, particularly in high-income countries.

EP-159-28 Geospatial analyses of *M. tuberculosis* transmission in Greater Gaborone, Botswana: the Kopanyo Study

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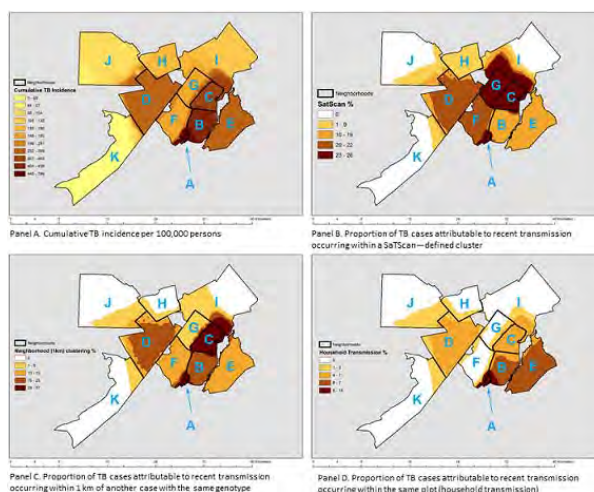
Background: International tuberculosis prevention and care guidelines recommend targeted testing and treatment of persons at highest risk of tuberculosis and those likely to progress from latent infection to active disease. Geographically targeted interventions have been suggested as a potential strategy. Since those who have been recently infected are at greatest risk of progression to active disease, we sought to identify neighborhoods in Gaborone, Botswana with the highest tuberculosis incidence and the highest percent of cases attributable to recent transmission.

Methods: As part of a multiyear molecular epidemiologic study, all culture-confirmed cases of tuberculosis registered in Gaborone, Botswana from September 2012–March 2015 were eligible for enrollment. *M. tuberculosis* isolates collected for the study were genotyped by 24-locus Mycobacterial Interspersed Repetitive Units-Variable Number Tandem Repeats (MIRU-VNTR). Residences of participants were mapped using ArcGIS. Recent transmission was defined as ≥ 2 persons with *M. tuberculosis* isolates with matching MIRU-VNTR (genotype-cluster). We calculated the proportion of cases attributable to putative recent transmission that occurred within statistically significant spatial scans (SaTScan-defined clusters), living within 1 kilometer of a genotype-clustered case (neighborhood transmission), and living in the same plot as a genotype-clustered case (household transmission). Cumulative tuberculosis incidence rates were calculated using 2011 Botswana Population and Housing Census data.

Results: A total of 1031 patients had an interpretable tuberculosis genotype and primary residence geocoded in Gaborone. Neighborhood A had the highest cumulative tuberculosis incidence rate (799 per 100 000 persons)

(Figure; Panel A). Neighborhood A also had highest proportions of recent transmission that occurred within SaTScan-defined clusters (24%) (Figure; Panel B), neighborhood transmission (37%) (Figure; Panel C) and household transmission (14%) (Figure; Panel D).

Conclusions: Tuberculosis incidence and transmission appeared to be geographically focal. Neighborhoods with the high rates and proportion attributable to recent transmission may be attractive locations for focused targeted testing and treatment interventions.



EP-160-28 Utilization of the WHONET program for early identification of *Mycobacterium tuberculosis* clusters based on molecular data

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Background: WHONET is free Windows-based database software developed for the management and analysis of microbiological, epidemiological and clinical data with a special focus on antimicrobial susceptibility test results. WHONET supports participation of national surveillance programs in the Global WHO AMR Surveillance System (GLASS), <http://www.who.int/drugresistance/whonetsoftware/en>. The implementation of SaTScan modules into WHONET allows the identification of clusters by various algorithms, for example Space-Time permutation. The aim of this study is to assess the feasibility of using the WHONET program as an aid for early identification of putative *Mycobacterium tuberculosis* clusters, based on molecular data such as results from MIRU-VNTR typing and spoligotyping.

Methods: We created an integrated Excel database containing epidemiological, microbiological and molecular data of Israel *Mycobacterium* National Reference Center laboratory confirmed *M. tuberculosis* cases for the years 2008–2013. In total, 1516 laboratory confirmed cases were included in the database. The database

was converted to WHONET 5.6 format by the BacLink2 program. Various user-defined non-conventional fields were added to the *M. tuberculosis* program like SIT, CLADE, 24 MIRU-VNTR and 43-spacer spoligotyping.

Results: By applying the Space-Time permutation algorithm to the database using 24 MIRU-VNTR and sample collection dates we identified six statistically significant clusters of *M. tuberculosis*. Interestingly, these clusters were previously identified by manual interrogation of the database. All the clusters were further analyzed against our complete up-to-date *M. tuberculosis* molecular database. Three of the clusters were found to be limited in time, size and space. The other three clusters are continuing and new cases still appear. Detailed description of the clusters will be discussed in the lecture.

Conclusions: To the best of our knowledge this is the first utilization of the WHONET - SatScan program for analyzing MTB molecular epidemiology data for identifying *M. tuberculosis* clusters. We are convinced that this may improve our capabilities for early detection of *M. tuberculosis* outbreaks. Regarding our promising results, we intend to expand the use in this program for other National Reference Centers in order to improve our surveillance capabilities.

EP-161-28 Phylogenetic diversity of *Mycobacterium tuberculosis* complex in Botswana

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Background: *Mycobacterium tuberculosis* complex (MTBC) is comprised of phylogenetic lineages that are differentially distributed globally. We aimed to describe MTBC diversity in Botswana and compare prevalence of lineages between urban Gaborone, the capital city, and rural Ghanzi, home of the indigenous San population.

Methods: As part of a multi-year prospective molecular epidemiology study, we performed genotyping by 24-locus Mycobacterial Interspersed Repeat Unit-Variable Number Tandem Repeat typing on sputum culture-confirmed cases of tuberculosis from 9/2012-8/2015 in Ghanzi and Greater Gaborone districts. Approximately 86% of TB cases during the study period had strains genotyped. We built an unweighted pair group method with arithmetic mean (UPGMA) phylogenetic tree using study strains and 184 international reference strains (<http://miru-vntrplus.org>). Phylogenetic lineage was determined by comparing the tree placement of study strains relative to reference strains and large sequence polymorphism-derived lineage names were assigned.

Results: Among 1617 strains with interpretable genotype, 1289 were among cases in Gaborone and 328 were among cases in Ghanzi. In Gaborone, all four major phylogenetic lineages of *M. tuberculosis* were present: 86% were Euro-American (1108/1289), 7% East-Asian (93/1289), 6% Indo-Oceanic (77/1289), and 0.8% East-

African Indian (10/1289); there was one case of *M. bovis*. In Ghanzi, 98% (320/328) of strains were Euro-American lineage, 0.6% (2/328) were Indo-Oceanic and 1.5% (5/328) were East Asian. A single Euro-American lineage strain accounted for 38% (126/328) of all cases in Ghanzi.

Conclusions: Euro-American is the dominant MTBC lineage in Botswana. Both phylogenetic and strain diversity are lower in Ghanzi, suggesting more insular TB transmission than in Gaborone. Different approaches to effective TB care and prevention may be required: comprehensive case-finding and treatment for active and latent TB infection may be expected to curb the TB epidemic in Ghanzi, whereas approaches to the TB epidemic in Gaborone may need to be adapted to address ongoing importation of TB.

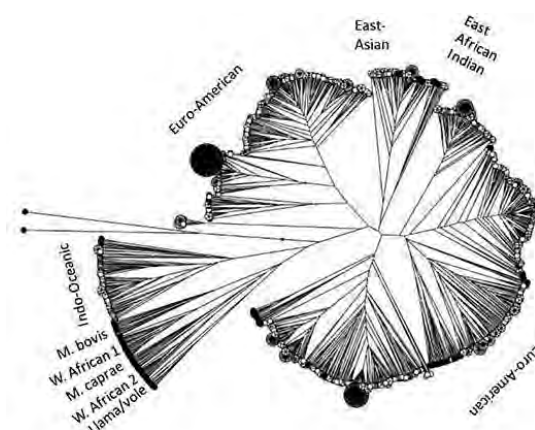


Figure1: Unrooted UPGMA tree of strains from Gaborone, Ghanzi, and the reference strain collection of <http://miru-vntrplus.org>. Ghanzi strains are shown in grey, Gaborone strains in white, reference strains in black.

EP-162-28 Potential of a combined technique of social network analysis and geographic information system in understanding transmission of *M. tuberculosis*

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Background: Epidemiological links among tuberculosis (TB) patients in the same genotype cluster are not always identified. Increasing attention is being paid to Social Network Analysis (SNA) and Geographic Information System (GIS) as complementary tools to assist molecular genotyping in understanding transmission patterns of *M. tuberculosis*. We aimed to evaluate the utility of SNA and GIS, combined with molecular epidemiology.

Methods: Bacillus-positive TB patients notified in Shinjuku City, Tokyo, Japan, from 2002 to 2012 were enrolled, and their demographic and clinical data, IS6110-RFLP data, and information regarding places they frequent were collected. Socio matrix was created to visualize and calculate degree centrality for each district. Degree centrality was defined as the number of TB patient incident upon a districts. The spatial features of

degree centrality of districts was evaluated using GIS to estimate the possible TB transmission site.

Results: The data of a total of 1026 TB patients were analyzed. A total of 106 genotype clusters consisting of 494 TB patients were identified; largest cluster consisted of 29 patients. Genotype clustering rate was 37.8%. Among the total 152 districts in the city, 126 districts were cited by the patients as their home or an area where they frequented. Average degree centrality of those 126 districts was 9.9. Districts with higher degree centrality were located in the west side of the city, indicating an area where TB patients tended to concentrate. In the largest genotype cluster consisting of 29 patients, 5 patients shared a district with the highest degree centrality (score 79). Several other districts were also shared among patients within the same cluster. Epidemiologic links among these patients had not been identified in the initial investigation.

Conclusion: Our result indicate that districts with high degree centrality could be important areas in considering epidemiological links of patients who have same genotype strains.

Figure Network of socio matrix

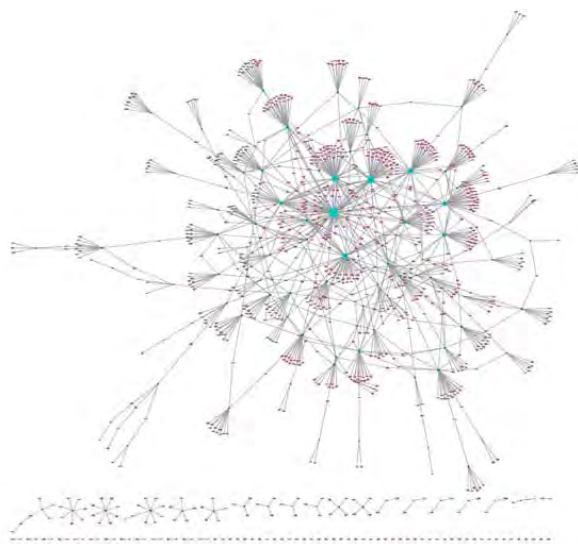


Figure. Network of socio matrix. Circles: tuberculosis patients, circles with red edge: tuberculosis patients who belong to any genotype cluster, squares: districts in Shinjuku, ties: connections of tuberculosis patients and districts

EP-163-28 Whole genome sequencing to analyze the transmission dynamics of multidrug-resistant *Mycobacterium tuberculosis* strains in Saudi Arabia

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Background: Globally, the major challenge in controlling the tuberculosis (TB) pandemic is the rise in drug resistance, specifically multidrug-resistant (MDR) and

extensively drug resistant (XDR) strains. Very little is known about the scope of historical drug resistance and ongoing transmission of resistant strains in Saudi Arabia. The country faces a moderate annual burden of TB, including the presence of 4% MDR. Considering the cosmopolitan population structure of the country, recent molecular studies showed ongoing transmission of TB involving the local and immigrant population. We therefore employed whole genome sequencing to study the TB transmission and MDR-TB dynamics in Saudi Arabia.

Methods: To define the transmission dynamics of MDR-TB, 69 phenotypically confirmed MDR isolates with demographical and clinical data were collected from different regions of the country. All the isolates were subjected to spoligotyping and MIRU typing followed by whole genome sequencing.

Results: Demographical data showed the predominance of Saudi nationals (66.7%). Almost 92.7% of the cases were pulmonary. Pan resistance to first line drugs was noticed among 59.4% of the cases which points the upcoming possibilities of emergence of XDR-TB. Predominating lineages were Clade I (30.4%) followed by Delhi/CAS (21.7%), Beijing (14.5%), Cameroon (11.6%) and EAI (10.1%). A combined data analysis of the traditional genotyping methods showed a clustering of 32 isolates into 7 groups while whole genome sequencing obtained 9 clusters. The overall cluster rate was 46.3%, which is extremely high. Interestingly, the Saudi population showed a cluster ratio of 65.6% with higher predominance of Clade -I, compared to the immigrants.

Conclusion: In the first whole genome sequencing based analysis of MDR-TB in Saudi Arabia, it was evident that the country faces the serious threat of ongoing transmission of MDR-TB with a higher predominance of historical Clades of *Mycobacterium tuberculosis* among Saudi nationals. The extreme level of strain clustering shows acquired resistance is not as high as expected and warrants focusing more on eliminating the transmission cycle.

EP-164-28 Evaluation and expansion of genome-based transmission chain estimation of drug-resistant *Mycobacterium tuberculosis* strains

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Background: The growing rate of drug resistant (DR) strains of *Mycobacterium tuberculosis* circulating within endemic areas makes understanding transmission dynamics of this bacterium a priority. Current research methods are relying more heavily on whole genome sequence (WGS) analysis for understanding the evolution and spread of pathogens. This necessitates an under-

standing of how WGS data can estimate transmission patterns of DR *M. tuberculosis* isolates.

Methods: Using 324 *M. tuberculosis* genomes isolated in Kinshasa between 2005 and 2010 we explored the computational approaches to estimating likely recent chains of transmission of DR strains from WGS data. Lineage and spoligotype patterns were estimated from WGS data using SpoType and the SpoNC method (spoligotype with pncA mutation clustering) was undertaken to look at improved resolution from the addition of one gene. Clustering analysis was then undertaken with currently used SNP cut-offs: >12 SNPs to exclude from a transmission chain and <5SNP as highly likely to be within a recent chain of transmission. These SNP cut-offs were augmented in 2 novel ways: removing DR-related sites for the SNP distances, as selective antibiotic pressure can artificially increase this distance, and a method called clade inclusion, which includes extra members of a likely transmission chain based on whether their common ancestor is known to be part of a transmission cluster in this dataset.

Results: Several common lineages and spoligotype families were found to be circulating within the Kinshasa region, including lineage 5, more common in West Africa, and lineage 4.7, rarely found elsewhere. Extension of SNP clustering methods increased clustering rates at the 5 SNP cut-off from 23% to 27%, indicating current methods likely underestimate transmission and clustering rates of DR *M. tuberculosis* strains. However, discordances between the Spoligo/MIRU standard and multiple SNP clustering methods show that specific cut-off values may not be suitable for valid estimations of transmission.

Conclusions: This work indicates that extension of current SNP clustering methods is likely to improve indications of transmission rates of drug resistant isolates. Further work is needed to truly explore the genomic markers and methods for estimation of *M. tuberculosis* transmission.

EP-165-28 Determining the transmission dynamics of tuberculosis in the Greater Banjul Area of The Gambia

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Background: *Mycobacterium tuberculosis*, the causative agent of tuberculosis (TB) is one of the most successful pathogens in the world. Although The Gambia is a TB endemic country, little is known about the transmission dynamics of the disease in the country. In the context of a TB household case contact study, we assessed the proportion of TB due to transmission within the household by genotyping isolates of patients and their diseased household contacts.

Methods: Contacts of index cases were followed up for two years for development of TB disease. With relevant

clinical features and a positive Mantoux test, sputum was collected; microscopy using Ziehl Neelsen and auramine staining was performed. Culture was done by the Bactec 9000MB or MGIT 960. Positive cultures were confirmed by standard methods and whole genomic DNA extraction was done for spoligotyping and MIRU VNTR.

Results: Out of 1137 index cases and 6436 contacts, who were recruited between 2002 and 2011, and were followed for 2 years for the development of TB disease, there were 106 bacteriologically confirmed secondary cases. By spoligotype analysis of 140 isolates from index and secondary cases from same households, 86 isolates (61.4%) are similar or differed by maximum one spacer, suggesting chains of transmission within households. However, when these similar spoligotypes were subjected to MIRU VNTR, a higher resolution technique, only 29 of 86 isolates (33%) of the paired isolates had similar MIRU profiles (up to one locus different), suggesting that only one third of all TB transmission occurred within the household.

Conclusions: The majority of TB transmission in The Gambia occurs in the community, outside households. These findings imply that public health efforts to decrease TB incidence may have limited impact if solely focused on household contacts, and that we urgently need better tools to identify where TB is transmitted in the community.

EP-166-28 Genetic diversity of *Mycobacterium tuberculosis* isolates by fingerprinting method in southern Iran

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Background: Genotyping methods for *Mycobacterium tuberculosis* are useful as molecular epidemiology tools that contribute to a better understanding of transmission. Information about genetic relatedness of isolates obtained during outbreaks can provide opportunities for prompt intervention. Random amplified polymorphic DNA (RAPD) analysis is a less specific method of producing DNA fingerprints. The aim of this study is to determine the relationship between 100 MTB isolated strains using RAPD-PCR based on genomic fingerprinting.

Methods: Template DNA was extracted from a 1.0-ml cell suspension of each strain by boiling method. The concentration of each DNA template was determined and adjusted to 25-50ng then subjected to RAPD PCR. The PCR amplifications for RAPD fingerprinting were carried out with 3 arbitrary primers 27F, 1525R and INS-2. The PCR products were separated by electrophoresis on 1.5% agarose gel. The NTSYS-pc software ver. 2.02 is used to estimate genetic similarities with the Jaccard's coefficient. The matrix of generated similarities is analyzed by the un weighted pair group method with arithmetic average. (UPGMA).

Results: By using of 1525R primer isolates were classified into 15 different groups. The largest group contain 21 isolates. By 27F primer 17 clusters were obtained and the largest cluster with 24 strains revealed diversity in geographical area. Primer INS-2 generated 25 different patterns for the isolates studied here.

Conclusions: RAPD analysis provided a rapid and easy means of identifying polymorphism in *M. tuberculosis* isolates, and it was found to be a valuable alternative epidemiological tool. In addition, the results of the present study showed heterogeneity in the *M. tuberculosis* strains in the population studied.

EP-167-28 Empirical measurement of the agent of tuberculosis transmission utilising the respiratory aerosol sampling chamber

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Background: *Mycobacterium tuberculosis* is purportedly transmitted by aerosolised infectious particles. In contrast traditional diagnosis and treatment monitoring is based on microscopy and culture of sputum which is of limited reliability for measuring infectiousness. We present the results from a novel experimental apparatus which mimics the circumstances of transmission in a controlled setting. The Respiratory Aerosol Sampling Chamber (RASC) measures and characterises respirable particles produced from tuberculosis patients accumulated over time.

Methods: 24 participants with drug-sensitive pulmonary TB diagnosed by GeneXpert were recruited from a high burden community in Cape Town, South Africa. Prior to initiating therapy each participant agreed to a one hour sedentary period in the RASC, a small, sealed, personal room of 1.4m³. The proportion of exhaled air from each participant built up to a median of 9.3% (range 6.8 to 10.4) in the chamber over a time period of 30 minutes or less. The air was subsequently sampled via an array of impactors and gelatine and polycarbonate filters allowing microbiological analysis both by culture and molecular methods.

Results: Bioaerosol sampling identified one or more colony forming units (CFU) in 10 of 24 (41.7%) participants. Of these the median was 2.5 CFU with a range of 1–14. The greatest yield was with the viable Andersen cascade impactor which gave a median concentration of 0.1 CFU per litre of exhaled air (range 0.04 to 0.57 CFU/L). Molecular methods yielded a positive droplet digital polymerase chain reaction (PCR) result in 21 of 24 (87.5%) patients. The median amongst

the positives was 132 genome copies with a range of 12 to 2468. The greatest yield was with a polycarbonate filter which gave a median concentration of 5.9 genome copies per litre of exhaled air sampled (range 0.9 to 54.8 copies/L).

Conclusions: We have empirically identified and quantified airborne organisms produced by active pulmonary TB patients under physiologically normal conditions. Airborne bioaerosols, when viable, represent the agent of TB transmission such that an individualised measure of infectiousness may be possible. This high sampling efficiency suggests the RASC may help further elucidate the dynamics between culture and PCR in TB transmission.

08. 'I need you': strengthening health systems

EP-168-28 Implementing standard operation procedures for tuberculosis case detection: a solution to tackle TB in 13 provinces of Afghanistan

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Background: Afghanistan has been failing to identify 45% (25 000) of the incident number of TB cases since 2006 and presumptive TB (P-TB) case identification in public facilities was 1.5%. This assessment explored the contribution of implementing standard operation procedures (SOP) on TB case notification in 13 provinces.

Intervention: TBCAP, TB-CARE I and Challenge-TB projects assisted NTP to develop/update national TB guidelines and SOPs for case detection and treatment, train health workers and on-the-job training, and provide supportive supervision. This led to a strengthened triage of clients; review of health facilities' performances; data analysis; and shared findings with primary health care implementing organizations and provincial health teams. The assessment team reviewed TB data from 2006–2015 and compared performance of 13 intervention and 21 other provinces.

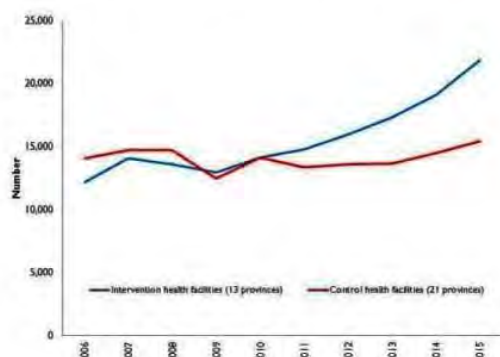
Results: During 2009–2015, 1.169 million P-TB patients attended health care facilities, 620 231 (53%) to 13 interventions and 549 704 (47%) to 21 provinces. In the intervention area, P-TB case identification improved by 186%, from 49 630 (2009) to 142 147 (2015). Bacteriologically confirmed TB case notification increased 42%, from 6139 (2009) to 8720 (2015); all forms of TB case notification advanced 69%, from 12 454 to 21 095. However, in 21 provinces, there was an 181% increase in P-TB patient identification: 19% for bacteriologically confirmed and 11% (13 545 in 2009 to 15 515 in 2015) for all forms of TB cases. The increase in TB case notification at intervention provinces was 80%;

though for 21 provinces, it was 10%, from 14 059 (2006) to 15 415 (2015) (Figure).

Conclusions and key recommendations: SOP implementation is an effective approach to increase access to TB service delivery to reach P-TB patients for screening, consequently, improving TB case notification for both bacteriologically confirmed and all forms of TB cases. We recommend the application of SOPs for TB case detection in countries with similar settings.

Figure Trends in TB case notification

Figure 1: Trend of TB case notification in intervention versus control provinces, 2006-2015



EP-169-28 Multi-stakeholder participation builds synergies to accelerate TB control

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Background and challenges to implementation: The public health sector cannot meet the End TB Strategy on its own. The medical, sociocultural, political, and financial dimensions of tuberculosis require the concerted action of different organizations, representing various disciplines, in the public and private sectors.

Interventions or response: With USAID/Philippines technical assistance, the provinces of Batangas (population: 2 710 816) and Misamis Oriental (population: 902236) in the northern and southern parts of the Philippines, respectively, organized a multisectoral alliance (MSA) to help implement the local TB control program. The initiative consisted of advocacy with and engaging institutions with the potential to participate in TB control; an orientation on TB, including its cause, transmission, control, and prevention, and cure; formulating a strategic plan that defined the MSA's organizational structure, the roles of each member, and their

projects and activities; and monitoring and mentoring. Members of the MSA represented schools and universities, private companies, hospitals, jails and prisons, faith-based organizations, the Armed Forces, civic organizations, and professional medical societies.

Results and lessons learned: The Batangas MSA helped increase the number of local government units with policies supportive of the TB program from 18% (6/34) in 2012 to 59% (20/34) in 2015, the number of certified and accredited DOTS facilities from 8% (3/40) in 2013 to 58% (23/40) in 2015, and referrals from public and private partners from 14% (965/6,831) in 2013 to 30% (2,291/7,637) in 2015. From 2013 to date, the province's case detection rate consistently surpassed the national target of 90%, which it failed to meet prior to the MSA's existence. In Misamis Oriental, the Department of Education, an MSA member, tested 93 school children for TB and helped enroll six found positive for the disease. Twenty-one teachers diagnosed with TB during the annual physical examination were enrolled in treatment in the MSA's private member-hospital. The provincial jail has arranged with DOTS facilities for the diagnosis of 21(3.5%) of 585 inmates and the supply of anti-TB drugs for those found with TB.

Conclusion: The provincial MSA is a strategy that effectively musters individual strengths of participating stakeholders for synergistic TB prevention and control efforts.

EP-170-28 Strengthening coordination for TB control at all levels: experience of Challenge TB and the Global Fund in Nigeria

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Background: The Nigerian TB program is majorly funded by USAID and Global Fund through various implementing partners. Ensuring the principle of 3 ones (one work plan, one budget, and one M&E plan) is challenging especially at states levels. NTP at various levels have multiple projects that are partners specific, not harmonized and in most situations not linked to each other; planning and implementation are not efficient, not coordinated, and NTP loses the opportunity of ownership and leadership.

Aim: to describe the on-going processes of ensuring effective coordination among all partners supporting TB programs at all levels using simple platforms and management tools.

Methodology: Open discussion between NTP, USAID, GF; TB-HIV IPs and KNCV/CTB and GF principal recipients; Review, alignment and or integration of all existing coordination mechanism/meetings; development of standard TOR; development of dashboard for all partners' activities quarterly at national level and 12 states (co-located states for GF and CTB)

Results: Establishment of partners forum in all 12 states; alignment of national meetings in the following order: (GF-PRs meeting, GF- TAC meeting, USAID/CTB partners forum meeting, and planning cell meeting); the planning cell meeting takes the overall responsibilities for effective change based on the program performance. Both GF -PRs and KNCV/CTB project participate in each project work plan development; 12 states TB operational plans developed; there harmonized plans (alignment and completing) at national and 12 states and implemented joint supervision. After two-quarters, the 12 co-located states with this mechanism demonstrated improved implementation rate of activities; contributed over 46% of the cases notified in both quarter 3 & 5 respectively; better utilization of Xpert machines; better performance of childhood TB (>6%) and TB-HIV indicators HCT, CPT and ART uptake (96%, 84%, and 74%, respectively).

Challenges: Different cycles of planning and funding; negative impact of the interdependence-if output of one partner is input to the other partner because of delays or procurement processes; and differential philosophy of working with government among implementing partners.

Conclusion: Ensuring the implementation of the three principles will help states take ownership and provide effective leadership for the program.

EP-171-28 Trend and prospect of tuberculosis mortality rate in Brazil: contributions for the National Plan to End Tuberculosis

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Background: The World Health Organization launched in 2014 the End TB Strategy that targets to reduce the number of tuberculosis (TB) deaths by 95% by 2035, compared to 2015. This work aims to analyze the trend and prospect of the TB mortality rate in Brazil.

Methods: An ecological study of times-series was performed using data available in the Mortality Information System from 2001 to 2014. Applying the Poisson regression, a time trend was estimated and variables associated to TB mortality rate were identified for Brazil. Thus, a multiple model was obtained to predict the TB mortality until 2035. This prediction was conducted under two scenarios considering: 1) the stability in the values of the associated variables for TB incidence observed for 2014; and 2) the improvement of these variables.

Results: The TB mortality rate presented a decrease of 3% per year, diverting from 3.1% in 2001 to 2.2/100 000 population in 2014. It was estimated that in 2035 this rate will reach 1.17/100 000, which represents a reduction of 47% since 2014 (Figure). In addition to time series analysis, treatment loss to follow up was associated to TB mortality (IRR = 1.040; 95% CI 1.026–

1.054). A simulation of a 5% reduction in loss to follow up until 2035, would accelerate the rhythm of this decrease and, in a 21 years period, about 7 thousand TB deaths would be prevented in Brazil, reaching, in 2035, a 0.94/100 000 population (57.3% reduction since 2014). **Conclusions:** The results suggest that reduction of loss to follow up can be a key element for the TB mortality rate reduction. In this sense, primary care strengthening as the main driver of care given to the TB patient needs to be considered as an important strategy. For this, the development of evidenced based Plans is necessary to achieve the target.

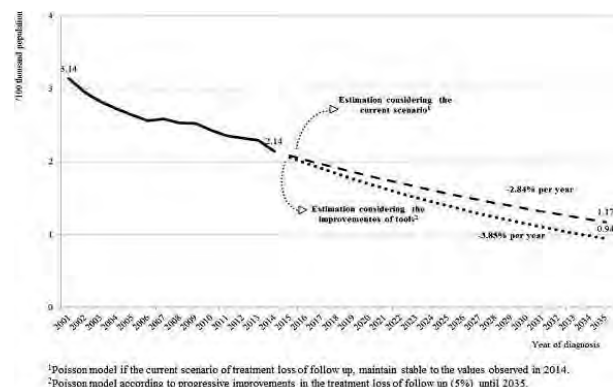


Figure 1 – Tuberculosis mortality rate: observed and estimated values. Brazil, 2011 to 2035.

EP-172-28 Effect of wellness-based health promotion and education on the demand for TB and other disease screening services

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Background: Healthlife (Wellness) defined as total whole person well-being is gaining recognition in Swaziland. Private companies, NGOs, and the government are spearheading wellness based health promotion and education to increase demand for screening services for HIV, TB, and other chronic diseases. An assessment of the effect of wellness based VS. disease based health promotion and education on demand for disease screening services was conducted in some companies in Swaziland

Study objectives: To assess the effect of Wellness based health education on the demand for TB screening services in some private companies in Swaziland.

Methods: This assessment used a comparative retrospective study design. Demand for TB screening data during disease based health education and after wellness based health education was collected and compared to analyze workers' attitude to TB and other diseases screening services

Results: It was noted that people gladly accepted TB-HIV prevention and other disease information when presented in the holistic Healthlife approach. There was also a significant voluntary willingness (98%) to test for TB/HIV and take up ATT/ARTs after Healthlife Manage-

ment workshops in the assessed companies as compared to estimates of 50% willingness to test for TB-HIV during the period of disease based health education.

Conclusion: Most people want to maintain physical well-being and are willing to screen for TB-HIV and get treatment as they saw this as a means to maintain wellness not only to prevent disease. Wellness based health education has a significant positive effect on demand for disease screening services

Recommendations: Organizations should invest in wellness based health promotion and education for their workers to increase uptake of TB-HIV and other disease screening services and prevent chronic diseases that lower work performance.

EP-173-28 How does the Global Fund impact on managerial capacity to achieve targets for tuberculosis management in Sri Lanka?

Qualitative insights

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Background: The Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM) has supported the National Tuberculosis (TB) Programme in Sri Lanka since 2003, using performance-based payments as their key disbursement mechanism. Middle level managers are tasked with tuberculosis prevention, patient management, supply chain, recording, reporting, monitoring and evaluation as part of the GFATM activity implementation at district and central level. Despite considerable funding inputs, the programme targets for TB case management have not been reached: a sharp drop in case notifications was recorded in 2012, reflecting the lapse in TB control activities.

Methods: In-depth, semi-structured interviews were conducted with 19 middle level managers drawn from key areas of the TB control program including clinical, laboratory, drug, information, and project management. The interviews explored four thematic areas of management capacity: personnel capacity (knowledge, skills, and attitudes); workload; facility and support service capacity; and systems and structural capacity.

Results: The GFATM's intensive reporting mechanisms and rigid deadlines have placed additional administrative workload on managers, negatively affecting their specialist areas of expertise, monitoring and supervision capacity. Financial assistance for new diagnosis technologies and uninterrupted drug supply have strengthened TB service delivery. However, the programme has experienced challenges in sustaining diagnostic services and information systems due to the high turnover of project staff recruited under GFATM funds, who are demotivated by low salaries and limited benefits. Delayed disbursements and funding gaps have created challenges in ensuring timely and consistent service delivery. GFATM's lengthy negotiation procedures and cumbersome implementation conditions have further hindered urgent recruitments and procurements.

Conclusions: Over the past decade, GFATM has focused on building technical capacity among managers in the area of service delivery, but has provided limited inputs to developing managerial leadership skills. The increase in bureaucratic procedures introduced by the GFATM in Sri Lanka's national TB programme has negatively affected middle level managers' performance, and may help to explain the programme's limited capacity to absorb funds effectively as well as poor outcomes. Introduction of more efficient and flexible project cycles as well as appropriate capacity building programmes for this cadre will be vital in looking towards New Funding Model.

EP-174-28 Contribution and cost of electronic monitoring of medication adherence for tuberculosis treatment in an urban Moroccan setting

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Background: In certain urban areas of Morocco, TB incidence can be two to four times the national incidence estimate and treatment default and non-compliance can be as high as 15%. This phenomenon is attributable to a wide range of health services and socio-economic factors such as lack of and barriers to quality primary health care services, poverty and health illiteracy. A compendium of mobile-health (m-health) solutions with real-time treatment monitoring, and health awareness programs can have great potential to improve TB treatment completion.

Intervention: From April 2014, we implemented Medication Event Monitoring System (MEMS) along with tailored adherence-promoting programs in select public health clinics in Salé and Skhirat-Témara, Morocco, priority regions for TB control. Newly diagnosed sputum smear positive (SS+) TB patients were approached to participate in the program on a voluntary basis. Those agreeing to participate were provided with Smart Pillboxes (SPs). SPs are equipped with programmable daily voice reminders and wireless network card through which patient-specific medication data are transmitted in real-time to MEMS. Patients identified in MEMS for not taking the medication are reminded via phone calls or household visits. Periodic TB campaigns and education sessions were also held in respective communities to raise awareness of TB and available health resources.

Results: As of February 2016, a total of 511 SSM+ patients participated in the program. Through September 2015, 251 patients completed treatment using SPs resulting in 98% treatment success rate (1 default, 1 treatment failure, 3 deaths). A total of 18 workshops, MEMS training, and program education sessions were

provided to nurses and relevant stakeholders of the project. Total economic costs of program implementation in the first five clinics (181 patients) was \$51 223 (2014 USD), translating into US \$283 per patient completing TB treatment under the SP program.

Conclusions: Initial findings of our m-health program demonstrate potentially a cost-effective solution to address treatment default and non-compliance problems in the urban Moroccan setting. Use of SPs and real-time treatment monitoring with MEMS presents an opportunity for individualized, patient-centered care. However, it must be followed-up with an array of patient care and education programs to ensure TB treatment completion.

EP-175-28 Opinion leaders: unengaged key stakeholders in TB care and prevention

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Background and challenges to implementation: How empowered people with TB and communities are may well be the rate-limiting factor for the Tuberculosis Control Programme.

Intervention or response: A baseline and midline KAP survey was done in 2011 and 2013 respectively in Global Fund Project Axshya. For maintaining comparability, similar methodology was adopted was similar in both surveys. 30 out of 374 Project districts were selected by stratified cluster sampling technique. Stratification was done as per North, South, East and West zone. Number of districts in each zone was selected in proportion to distribution of 374 districts in respective zones. In each district 10 Primary Sampling Units, villages for rural areas and wards for urban areas, were selected by Population proportional to size sampling procedure. The Urban Rural ratio was maintained as per district's actual ratio. House listing done in every PSU provided necessary sampling frame. Two Opinion leaders in each PSU were approached and those who consented were interviewed. The types of opinion leaders interviewed were Village Pradhan, Panchayat Member, Ward Member, Religious Leader, Auxillary Nurse Midwife, Aangan Wadi Worker. A total of 511 opinion leaders were interviewed in Baseline survey and 611 in the midline survey.

Results and lessons learnt: More number of opinion leaders were aware that cough of over 2 weeks is key symptom of TB in midline (88%) than in baseline (78%) and know that treatment of TB is through allopathic medicines in midline (86%) than in baseline (71%). However for all other key indicators like transmission of TB through air, sputum test for TB diagnosis and duration of TB treatment there was a decrease in proportions. Moreover only 17% played an active role in creating awareness for DOTS in midline as compared to baseline (22%).

Conclusions and key recommendations: Strategies involving opinion leaders' engagement for promoting TB care and prevention holds great promise of being

effective for developing countries like India, but the effort been sub-optimal. NTP needs to acknowledge the role of opinion leaders and engage with them as they are pivotal in the End TB Strategy.

EP-176-28 Development of the patient care system to reduce defaulting among migrant tuberculosis patients along Thai-Myanmar border

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Background and challenges to implementation: High treatment default rates had been observed among smear-positive tuberculosis patients in migrant populations. In 2013, the default rate was reported as 18.75% (12/64). This rate was much higher than WHO recommendation (5%).

Intervention or response: This action research was to evaluate the rate of default among smear-positive tuberculosis patients who participated in the intervention. The study was carried out in a tertiary 350-bed hospital near Thai-Myanmar border which is situated with shops and business. The intervention was provided to 73 consecutive smear-positive migrant tuberculosis patients registered from October 2013 to September 2014. The intervention included: 1) patient-centred care planning with multidisciplinary team approach, 2) One-stop service in TB clinic, 3) referral system linking hospital with community, 4) a referral system for follow up care in Myanmar, and 5) DOT and home visits by migrant volunteers. Data was collected from the TB register and entered into SPSS. Frequency, percentage, mean, standard deviation were used for data analysis.

Results and lessons learnt: Over half of patients were male (61.64%) and average age was 35 years. Patients were registered as 69 new smear-positive, 2 relapse and 2 treatment after failure. All patients knew their HIV status and 16.44% had HIV infection. The default rate was 6.84% and death rate was 2.7%. Patient satisfaction at the end of treatment was 82.2%. 80.6% patients were able to perform self care correctly and four migrant tuberculosis patients were referred for follow up care in Myanmar.

Conclusions and key recommendations: The multidisciplinary teams have cooperated in the treatment of migrant tuberculosis. Through the forwarding of data, a referral system, DOT and home visits by migrant volunteers, the default and died rate have decreased. This method is recommended in the care of migrant tuberculosis patients. It could be concluded that through the development of the patient care system for migrant tuberculosis patients, the default and died rate decreased. Therefore, this concept should be applied for migrant tuberculosis patients.

09. GenXpert: exciting results from field implementation

EP-177-28 Contribution of GeneXpert implementation towards detection of multidrug-resistant TB in Uganda

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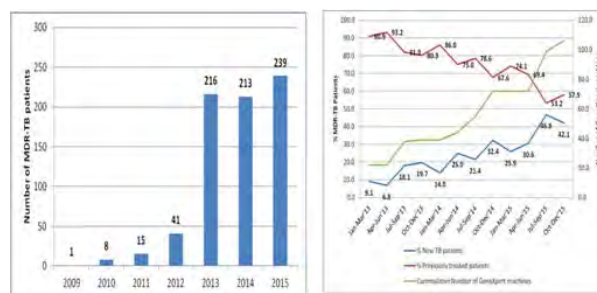
Background and challenges: The estimated prevalence of multi-drug resistant tuberculosis (MDR-TB) in Uganda is 1.2% among new TB patients and 12.1% among previously treated patients. Until 2012, MDR-TB was mainly diagnosed using culture and drug susceptibility testing at the National TB laboratory, an 8-12 week turnaround time for results. Consequently the MDR-TB case detection rate was low.

Interventions: With funding support from The Global Fund, PEPFAR, and implementing partners, Uganda initiated GeneXpert implementation progressively reaching 106 machines country wide. The MOH/NTLP algorithms for using GeneXpert specifies previously treated TB patients, HIV-infected presumptive TB patients, children, pregnant women, health workers, prisoners, and refugees. Samples of patients diagnosed with Rifampicin Resistance were sent for culture and DST and patients started on MDR-TB treatment. We examined the contribution of GeneXpert testing towards MDR-TB case detection and categorized the patients by history of exposure to TB treatment.

Results and lessons: 668 MDR-TB patients were detected during GeneXpert implementation, compared to 65 patients prior to introduction of the technology, a 10-fold increase. With GeneXpert testing, the proportion of new TB cases among all MDR-TB cases detected increased to 47% in one quarter, while the proportion of previously treated TB cases steadily decreased from about 91% before GeneXpert to 53% in the same quarter. These results highlight the burden of undetected rifampicin resistance among newly diagnosed TB patients that are not routinely tested using GeneXpert. This undermines efforts to combat MDR-TB.

Conclusion: Confronting TB drug resistance through prevention and early detection requires testing using GeneXpert all new bacteriologically confirmed TB patients irrespective of HIV status. We recommend further research to determine the prevalence of rifampicin resistance among all presumed TB patients, and increased investment in GeneXpert implementation.

Figure Left: MDR-TB patients enrolled annually. Right: MDR-TB detection by previous exposure to TB treatment



EP-178-28 Increased diagnostic yield and notifications of bacteriologically confirmed cases using Xpert® MTB/RIF as the initial test in semi-pastoralists: Ethiopia

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Background: In Ethiopia, a high tuberculosis (TB) burden country, Xpert MTB/RIF is currently recommended as the initial test for children <5 years, presumptive drug-resistant TB cases, some risk groups and sputum smear-negative people living with HIV. All other sputum smear negative (SSN) presumptive cases are given an antibiotic trial, and/or clinical examination. A reliance on low sensitivity sputum smear microscopy (SSM) as the initial test disproportionately affects pastoralists/semi-pastoralists, who have a higher prevalence of TB than the general population (291 vs. 240 per 100 000), lower case notification rates and limited access to services. This study aims to provide evidence for the categorization of semi-pastoralists/pastoralists as a key population eligible for Xpert MTB/RIF as the initial test, by assessing additional diagnostic yield, and impact on bacteriological confirmed notifications in this population.

Study objectives: 1) To assess the diagnostic yield of Xpert MTB/RIF among SSN presumptive TB cases within an active case-finding strategy in semi-pastoralist Bale Zone, Ethiopia, and 2) To assess the impact of Xpert MTB/RIF on the proportion of bacteriologically confirmed cases notified within an active case-finding strategy in semi-pastoralist Bale Zone, Ethiopia.

Methods: As part of a comprehensive active case-finding intervention, Xpert MTB/RIF was introduced in Bale Zone, Ethiopia. Presumptive cases provided two sputum specimens. SSM was performed, with Xpert MTB/RIF provided to all SSN presumptive cases on the same day. The proportion of bacteriologically confirmed cases notified during the intervention period was compared with the pre-intervention period where Xpert MTB/RIF was not available. The diagnostic yield of Xpert MTB/RIF was additionally calculated.

Results: Of 1686 SSN presumptive cases, 14.3% (242) were positive for TB with Xpert MTB/RIF. The proportion of bacteriologically confirmed TB cases notified before Xpert MTB/RIF was introduced was 33.8% (715/2114), compared with 42.1% (1266/3003) after introduction ($P < 0.0001$).

Conclusions: Xpert MTB/RIF increased diagnostic yield by 14.3% among semi-pastoralists in Bale Zone. The assay contributed to a 8.3% increase in the proportion of bacteriologically confirmed cases notified. Xpert MTB/RIF should be considered as the initial test for key pastoralist/semi-pastoralist populations in Ethiopia.

EP-179-28 Does the clinical performance of new tuberculosis diagnostic tools meet the required performance standards under programmatic conditions?

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Background: The tuberculosis control program of Rwanda is currently phasing in light emitting diode-fluorescent microscopy (LED-FM) as an alternative to Ziehl-Neelsen (ZN) smear microscopy. This, alongside the newly introduced Xpert (Cepheid, Sunnyvale, CA, USA), is expected to improve diagnosis of tuberculosis and detection of rifampicin resistance in patients at health facilities. However, the incremental diagnostic yield conferred by these new diagnostic tools over existing ZN smear microscopy under programmatic conditions is unknown.

Methods: This was a cross-sectional study involving four laboratories performing ZN and four laboratories performing LED-FM microscopy. The laboratories include four intermediate (IL) and four peripheral (PL) laboratories. After smear microscopy was done at these laboratories, the remaining samples, of a single early-morning sputum from 648 participants, were tested at the National reference laboratory (NRL) using Xpert and mycobacterial culture as a reference standard.

Results: A total of 96 participants were culture positive for *M. tuberculosis*. The overall sensitivity, PL, for ZN was 55.1% (48.2–62%), LED-FM was 37% (30.2–43.8%) and Xpert was 77.6% (72.8–81.2%) whereas for IL, ZN was 58.3% (47.7–68.9%), LED-FM 62.5 (54–70.9%) and Xpert 90 (85.9–94%). The incremental sensitivity (IS) of Xpert from ZN to LED-FM, was 31.1%; $P = 0.015$ and 34.3%; $P = 0.007$ among PL and IL, respectively. The IS of Xpert was statistically significant for both smear methods at PL (32.9%; $P = 0.001$) but not at the IL (30%; $P = 0.125$).

Conclusions: Our study findings of the early implementation of the LED-FM did not reveal significant increment in sensitivity compared to the method being phased out (ZN). However, a significant incremental

sensitivity for Xpert from both smears methods supporting its recommendation as an initial diagnostic test TB suspects. The findings of this evaluation should be supported with further studies measuring clinical outcomes in patients tested with the alternative diagnostic test strategies.

EP-180-28 Implementation of GeneXpert® technology for rapid TB diagnosis in South Sudan: lessons learnt

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Background and challenges to implementation: The World Health Organization estimates the prevalence of multidrug-resistant tuberculosis (MDR-TB) among new and retreatment TB cases at 2.2% and 11%, respectively (WHO Global tuberculosis report 2015). The Central Reference Laboratory (CRL) is not fully functional, though 27 MDR-TB cases have been diagnosed since 2010 through the support of CRL in Kenya. The use of GeneXpert testing is a new concept in South Sudan. The GeneXpert algorithm includes screening of TB among PLHIV, retreatment cases, failure of treatment at 5 and 6 months, MDR suspects, and MDR contacts. Laboratory technicians at the CRL were trained on GeneXpert use. Two machines and 1200 cartridges were procured, and testing started in January 2015. By July 2015, only 80 samples had been tested using the GeneXpert machine.

Intervention or response: To increase GeneXpert testing, an accelerated plan was developed, and the algorithm was modified to include smear negative presumptive TB cases. Transporters and health care workers from the 3 TB diagnostic centers in Juba were trained in sputum sample handling and basic TB knowledge. A TB Sample Referral System (TSRS) using motorcycle to transport samples was developed. Two sputum samples were provided from each patient; the rifampicin resistant sample was referred to Kenya for culture and Drug Sensitivity Test (DST). Feedback results for GeneXpert testing are provided within 24 hours after the samples are received at CRL, and are delivered by motorcycle the following day to the respective TB Management Units (TBMUs).

Results and lessons learnt: 973 samples were tested January–December 2015, of which 934 had valid results. 26.0% (242/934) of the valid results could not be categorized due to missing information. Rifampicin resistance was 0.7% among new patients, 11.3% among retreatment, 2.8% among PLHIV, and 2.1% in uncategorized patients. Among smear negatives, 36.1% (211/585) were bacteriologically confirmed using GeneXpert testing.

Conclusions and key recommendations: GeneXpert testing can help identify additional bacteriological confirmed cases among smear negative pulmonary cases. GeneXpert can expand access to TB diagnosis in high

burden areas and high HIV prevalence sites. Motorcycles are an effective way to transport samples in areas with no courier services and limited transportation systems.

EP-181-28 A tool to reduce treatment initiation delay

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Background: Bangladesh is sixth among the 22 TB high burden countries. Despite of this high burden of TB, DST/culture was the only way to diagnose MDR cases, which used to take at least 6 weeks. The National Tuberculosis Control Programme (NTP) Bangladesh with the support of the TB CARE II project introduced GeneXpert to diagnose drug resistant (DR) TB cases in early 2012 to rapidly diagnose and reduce the treatment initiation delay caused by the lengthy diagnostic method. The introduction of GeneXpert made it possible to diagnose a patient's drug sensitivity status within couple of hours; however, since the samples of the GeneXperts are transported from different places, it was not possible to deliver the report immediately after diagnosis, which was again a barrier to initiating treatment immediately. **Methods:** To reduce treatment initiation delay even further, the project introduced a mobile-phone based Xpert-reporting application at the Xpert laboratories to send test reports immediately after the result is available. Xpert reporting is a web based reporting tool that enables the lab technologists to enter GeneXpert results to a web application, to send the test results to the referral peripheral lab or physician from where the test sample was sent. The relevant patient was also electronically notified to collect the test result. Lab technologists use a tablet PC or smartphone to send this report and reports are sent to the recipient as a text message. A copy of the report goes to a database server and these data are used for data analysis, reporting and decision making purposes.

Result: Currently Xpert reporting has been being used in 26 GeneXpert labs throughout the country. Delay in treatment initiation has been reduced from up to 15 days to 1-2 days, since the referral lab is getting the result of a suspected MDR TB patient soon after the test is done.

Conclusions: Xpert-reporting has a significant potential to expedite treatment initiation of a MDR TB patient. With the help of Xpert reporting, it is possible to enhance the treatment success rate.

EP-182-28 Use of Xpert® MTB/RIF / GeneXpert® cycle threshold to replace monthly culture in the follow-up of MDR-TB patients in Bamako, Mali

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Introduction: World Health Organization (WHO) guidelines recommend sputum smear microscopy monthly culture during multidrug-resistant tuberculosis (MDR-TB) treatment. These recommendations face obstacles such as the lack of widespread availability of bio-safety compliant culture labs, resulting in long transportation times and high rates of contamination, and the long turnaround time for culture results (6/8 weeks). The Xpert MTB/RIF diagnoses the presence of *M. tuberculosis* in 2 hours, based on real time PCR on which the cycle threshold (Ct) is inversely proportional to ADN quantity present in the sample. So we hypothesize that the measurement of changes in the bacterial load in Xpert MTB/RIF is as good an indicator of second line treatment success as culture of mycobacteria.

Objective: Compare GeneXpert® Ct increase with monthly cultures in the follow-up of MDR-TB patients in Bamako, Mali.

Methodology: We conducted an approved prospective cohort study between March 2015 and February 2016, including all MDR-TB patients who have been diagnosed with Xpert MTB/RIF and started second-line treatment at the clinic. This multi-center study included three sites: the MDR-TB clinic at University Hospital of Point-G where samples were collected, INRSP/NRL for GeneXpert, and SEREFO for culture. MDR-TB patients were asked to provide 5ml of sputum samples each month for Xpert and culture.

Results: Thirty six patients were enrolled. The median age was 35 years, the sex ratio was 2.27 (25/11) and 11.11% (4/36) were coinfectd with HIV. For negative culture samples, the mean Ct value was 28. During the first 6 months of follow up, the mean Ct value was respectively 22.4 ($n=21$), 25.8 ($n=23$), 24.5 ($n=21$), 24.6 ($n=18$), 27.0 ($n=14$), 31.1 ($n=9$). Patients who failed to convert their culture by 5 months had average Ct values of 22.8 and patients who culture converted had average Ct values of 28.

Conclusion: The Xpert MTB/RIF can be used to follow MDR treatment. It is faster than culture and gives reliable results. In future studies with a larger sample size, the exact slope of the decrease in bacterial load that predicts treatment success can be calculated.

EP-183-28 Distribution of DR-TB following the nine revised criteria for Xpert® MTB/RIF testing in Bangladesh

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Background: One of the mandates of CTB Bangladesh is to promote proper maintenance and optimal utilization of all public sector GeneXpert machines for the diagnosis of drug-resistant TB (DR-TB). Since May 2015, the project has been supporting the NTP to refer all presumptive DR-TB patients to GeneXpert sites for Xpert MTB/RIF testing. The NTP revised nine criteria are: 1) failure of Category I; 2) failure of Category II; 3) symptomatic close contacts of DR-TB patient; 4) non-converters of Category II (remain positive at 3rd month); 5) non-converters of Category I (remain positive at 2nd month); 6) all relapses (Category I and II); 7) all treatment after loss to follow-up (Category I and II); 8) all HIV-infected persons, and 9) others, as determined by attending physician, which includes clinically diagnosed pulmonary and extrapulmonary TB. The objective of this research was to determine the proportion of *Mycobacterium tuberculosis* and rifampicin resistant TB (RR-TB) among presumptive DR-TB patients.

Methods: Data from all 50 668 presumptive DR-TB patients tested by Xpert MTB/RIF were collected from the 39 GeneXpert sites between October 2014 and December 2015. The proportion of MTB and RR-TB was calculated.

Results: Of 50 668 presumptive DR-TB patients, 36.4% (18 455) were diagnosed as *M. tuberculosis* and 2.27% (1,151) as RR-TB. The RR-TB patients were: 9.0 % (139) failures of Cat I, 6.7% (19) failures of Cat II, 2.3% (287) non-converters of Cat I, 5.1% (17) non-converters of Cat II, 6.6 % (389) relapses (Cat I and II), 5.3% (23) treatment after loss to follow up, 19.5% (33) close contact of MDR TB patient, 0.00% (0) HIV infected persons, and 0.83% (244) other.

Conclusions: Close contacts of DR-TB patients, failures of Categories I and II, and relapse cases should undergo Xpert MTB/RIF testing, as they have the highest proportion of RR-TB. Although very few patients in the 'other' category were found to have DR-TB, 15% had MTB, which was previously undetected. NTP should use this information to further refine testing algorithms to optimize case detection of both MTB and DR-TB.

EP-184-28 Scaling up Xpert® MTB/RIF implementation under India's Revised National TB Control Programme

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Background: In 2015, India's National TB Control Programme had 123 Xpert MTB/RIF sites including 30 sites in ART Centres in high burden settings and four sites in major cities to increase diagnosis for paediatrics. The program has the policy to use Xpert for diagnosis of presumptive drug resistance cases. Key population like people living with HIV/AIDS, paediatrics and extra pulmonary cases have been prioritized for testing by Xpert. We assessed the implementation of Xpert MTB/RIF under programmatic conditions.

Methods: Data on Xpert tests was collected in 2015 from 122 functional Xpert sites across 27 provinces on monthly basis using a standard tool consisting of information on laboratory performance.

Results: Of the 213 762 tests done across 122 sites, there were 45 922 (21%) PLHIV, 25 173 (12%) paediatric and 17 469 (3%) extra pulmonary samples tested. Valid tests were 201 597 (94.3%) and invalids were 12 165 (5.7%). Of the test failures there were Rif indeterminate (14.3%), Errors (44.2%), Invalids (27.9%), No results (13.6%). Of the valid tests, *Mycobacterium tuberculosis* was not detected in 110 665 samples (54.9%). *M. tuberculosis* complex was detected in 90 932 (45.1%), out of which Rif sensitive were 76 293 (83.9%), 9.5% HIV co-infected, 3% paediatric, 19% extra pulmonary TB. Rif resistance was detected in 14 639 (16.1%), 4.4% HIV co-infected, 3.0% paediatric and 3.0% extra pulmonary TB.

Testing for PLHIV ranged from 36-100% (median 86.5%) across 30 ART centres and 0-95% (median 20%) across the rest of the sites. Testing for paediatrics ranged from 95-100% (median 97.5%) across four paediatric project sites and 0-40% (median 7.5%) across the rest of the sites. Testing for extra pulmonary samples ranged from 0-77% (median 15%).

Conclusions: Public sector deployment of Xpert can have a great impact on diagnosis of tuberculosis and resistance to Rifampicin in key populations. The testing of PLHIV, paediatric and extra pulmonary cases varied across different sites. The NTP should involve different stakeholders, innovate in public private partnerships to increase testing of key population by rapid molecular diagnostics like Xpert. Overcoming logistic hurdles and availability of adequate trained manpower will ensure that Xpert laboratories are utilized to their full capacity.

EP-185-28 It's broken again: the scenario of GeneXpert® machines in Bangladesh

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Background: GeneXpert has revolutionized the diagnosis of drug resistant TB (DR-TB) by delivering rapid results without sophisticated laboratories. However, many countries report significant challenges during scale-up. USAID supported the Bangladesh NTP to install 39 GeneXpert machines between 2012 and 2014. Although DR-TB detection significantly increased during scale-up, it decreased in 2015 as machines began to malfunction. We analyzed the context related to GeneXpert malfunctions.

Methods: Investigators collected data between April 2012 and March 2016 from existing records of NTP, Challenge TB (CTB), TB CARE II, and Cepheid's local agency. They calculated turnaround time for replacing or repairing different components of GeneXpert machines.

Results: 80% of GeneXperts began to report modular failure, error code, or communication loss by one year post-installation. At any time, approximately 21% of modules failed and 26% of machines were non-functional. Replacement of modules and spare parts took between five and fourteen months. Mean time for machine calibration after installation was 20 months, and customs clearance for modules, cartridges, spare parts and GeneXpert check-kits ranged from 3 to 5 months. Slow resolution of issues was due to lack of local maintenance expertise; inadequate training; and lack of funding for ancillary equipment, repair, maintenance, and renovation. Turnaround time for incident reporting of up to four months was reduced to just six days after CTB intervention. Encouragingly, the situation improved with CTB support from September 2015 as machines were calibrated, UPS servicing time shortened, and onsite orientation provided. CTB engaged Cepheid's local agent to reduce customs clearance time from 3 to 8 months to 14 days, and turnaround time for module replacement to under 62 days. However, delays by Cepheid in sending new modules and spare parts persists.

Conclusions: Delayed manufacturer response greatly impedes programmatic efforts to enhance diagnostic capacity in Bangladesh. The current status of GeneXpert bodes poorly for further scale-up and sustainability. A more rapid response to machine malfunctions with in-country expertise and stronger monitoring and support through closer collaboration between NTP and Cepheid is imperative. In the absence of increased support, more robust diagnostic technology will be required for settings like Bangladesh to reach END TB targets.

ORAL ABSTRACT SESSIONS

10. HIV and TB: lessons from Africa

OA-372-28 Tuberculosis prevalence and incidence among people living with HIV attending HIV care and treatment clinics in Botswana, August 2012-October 2014

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Background: Botswana has a high tuberculosis (TB) HIV burden with the second highest HIV prevalence in the world of 18.5% and TB incidence of 385/100 000 population. Xpert MTB/RIF testing services, accompanied by training in intensified TB case finding, were introduced at 26 HIV Treatment Clinic (HTC) following WHO guidelines. We assessed the burden of TB among people living with HIV (PLHIV) during the first year of ART.

Methods: PLHIV attending HTC were interviewed, screened for TB symptoms and information abstracted from medical records at ART initiation and each clinic visit through 6-12 months of follow-up. Symptomatic patients provided sputum samples for testing by smear microscopy, Xpert MTB/RIF and culture. A TB case was defined as a patient with bacteriologic confirmation or having received anti-tuberculosis treatment (ATT). We assessed the prevalence of TB defined as patients on ATT at ART initiation or TB diagnosed within six months prior to ART initiation. New clinical episodes of TB while on ART or repeat TB episodes occurring after completing ATT were classified as incident cases. Cox proportional hazard regression was used to model TB incidence by pregnancy status among women.

Results: Among 6041 patients enrolled for ART initiation from August 2012 to March /2014, 4042 (67%) were female and 1173/404 (29%) were pregnant. The mean age was 35 years (range: 2 months-87 years), and median baseline CD4 was 247 cells/ μ L (interquartile range 139-320). TB prevalence was 3.6% (220/6041); there were 314 cases of incident TB over 5495 person-years (PY), yielding a rate of 5714/100 000 PY (95% Confidence Interval [CI]: 4498-7265/100 000 PY), see Table. Pregnancy was associated with an increased TB incidence among women (hazard ratio, 5.5 [95% CI 3.8-7.9]).

Conclusions: Prevalent TB among PLHIV initiating ART under current eligibility criteria in Botswana is high suggesting patients would benefit from earlier HIV treatment. As expected, incident TB declined over the first year of ART but remained elevated, underscoring the need for further TB prevention and control efforts.

Table. Incidence of Tuberculosis among People Living with HIV during the First Year of ART, Botswana 2012-2014

Quarter	Person-years (PY)	TB cases	Rate per 100,000 PY	95% CI
Q1	1368	142	10,378	8,804–12,200
Q2	1288	41	3,183	2,344–4,324
Q3	1103	45	4,078	3,046–5,463
Q4	873	50	5,727	4,340–7,556
Q5	862	36	4,173	3,010–5,786

OA-373-28 The infectiousness of HIV-seropositive tuberculosis patients in sub-Saharan Africa

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Background: Policy recommendations on contact tracing of HIV seropositive tuberculosis patients have changed several times. Current epidemiological evidence informing these recommendations is considered low-quality and prior studies have shown heterogeneous results. We assessed latent tuberculosis infection (LTBI) in household contacts of HIV seropositive and seronegative tuberculosis patients, evaluating three-way interaction with other variables. We also compared co-prevalent and incident tuberculosis in these contacts.

Methods: Adults laboratory diagnosed with either sputum culture or smear positive tuberculosis were identified from Old Mulago Hospital in Kampala, Uganda. Field workers visited case homes and enrolled consenting household members. LTBI in contacts was measured through tuberculin skin testing and a positive result was defined as an induration ≥ 10 mm for HIV seronegative contacts and ≥ 5 mm for HIV seropositive contacts. Relative risks were calculated using modified Poisson regression models with robust error variance. Standard assessments of interaction between LTBI, the HIV serostatus of the index case, and third variables were performed. Contacts were evaluated for tuberculosis disease at baseline and at six month intervals for 24 months.

Results: In total, 1912 household contacts of 499 tuberculosis index cases were enrolled. LTBI was found in 623/908 (68.6%) and 752/1004 (74.9%) contacts of HIV seropositive and seronegative tuberculosis cases (RR = 0.92, [95%CI, 0.85-0.99]). Upon further stratification, an interaction was found between LTBI, the HIV status of index cases and cavitory disease ($P < 0.0001$ for interaction) and smear status ($P = 0.009$ for interaction) of indexes. A multivariable model, controlling for family size, age and alcohol use of the contact, and smear and cavitory status of index cases, continued to show interaction. No other variables modified this relationship, including cough duration of the index ($P = 0.6138$

for interaction). Rates of co-prevalent and incident disease were similar amongst contacts.

Conclusions: This study suggests that HIV seropositive TB cases are only less infectious than seronegative patients when smear-negative or without cavitory disease. This finding may explain heterogeneity found in prior studies and, coupled with equal rates of disease in both contact groups, provide evidence suggesting that active case finding through contact tracing should include HIV seropositive index cases in high burden settings.

OA-374-28 Performance of CXR screening with molecular diagnosis for pulmonary tuberculosis in HIV-positive cases with no clinical symptoms in Kigali, Rwanda

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Background and challenges: The World Health Organization has recommended using sputum culture and Xpert MTB/RIF assay as the gold standard for diagnosing tuberculosis (TB) in HIV infected individuals. Rwanda, like most other countries in Sub Saharan Africa, is currently facing a burden of a human immunodeficiency virus (HIV) epidemic. In 2015, Rwanda reported a general HIV prevalence of 3% as recorded in the last Demographic and Health Survey. According to the last TB prevalence survey of Rwanda, the national TB prevalence for Rwanda recorded a national average of 119.3 in 100 000 for bacteriologically confirmed cases. Resource limited settings still struggle with diagnosing TB in HIV positive clients, as the current diagnostic tools are imperfect. All HIV-positive adults and adolescents should be screened for active TB infection at enrollment and regularly at each clinical encounter with a clinical algorithm. The objective of this public health activity is to assess the performance of chest X-ray screening combined with molecular diagnosis for pulmonary TB in HIV positive cases with no clinical symptoms

Intervention: This activity was conducted between August and December 2015. Screening for TB in HIV positive cases was done using mobile digital X-ray units was carried out with chest X-ray for abnormalities with optical and molecular diagnostic techniques for laboratory confirmation

Results and lessons learnt: A total of 15 186 HIV positive cases, of these 11 091 were screened for pulmonary TB using symptomatic and chest X-ray screening. The majority screened were females (64%). Among those with presumptive TB, 153 (8.4%) showed clinical symptoms with normal CXR, 1186 (65.0%) with suggestive chest X-rays but no symptoms, 485 (26.6%) both symptoms and suggestive chest X-rays. Cases with suggestive chest X-rays with no clinical symptoms contributed to 53.7% of 67 cases diagnosed with GeneXpert

Conclusion: The combination of chest X-ray for screening and GeneXpert as a laboratory diagnostic tool for an HIV-positive population increased diagnosis in patients without any obvious clinical symptoms for pulmonary TB

OA-375-28 Performance of WHO TB symptom screen in hospitalized HIV-positive Kenyan children

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Background: The WHO recommends TB screening of HIV+ children using a three-part symptom screen including cough, fever, and poor weight gain (report of weight loss or WAZ < -2) in conjunction with TB contact screening to determine eligibility for IPT. Performance characteristics of the pediatric WHO TB screen have not been widely assessed.

Methods: This study was nested within a randomized controlled trial in hospitalized HIV+ children (NCT02063880). Microbiologic confirmation of TB was ascertained in all children regardless of clinical TB symptoms via 2 gastric aspirate liquid cultures, 1 gastric aspirate Xpert MTB/RIF and 1 stool Xpert MTB/RIF. TB contact history and symptoms were collected. Confirmed TB was defined by a positive Xpert MTB/RIF or culture result. Diagnostic performance (sensitivity, specificity, PPV, NPV, and AUC) of TB symptoms and contact history to detect confirmed TB was assessed. Association of clinical symptoms and contact history with confirmed TB was determined using univariate logistic regression and χ^2 or Fisher's exact tests.

Results: Of 176 HIV+ children with microbiologic TB test results, 14 (8%) had confirmed TB (95%CI 4.4-13). Median age was 1.9 years (IQR 0.96-4.78) and median CD 4% was 14.9%. Report of weight loss and history of TB contact were associated with confirmed TB [OR 12.0 (95%CI 2.59-55.5); $P < 0.0001$ and OR 4.35 (95%CI 1.31-14.42), $P = 0.02$, respectively]. Poor weight gain, fever and cough were not associated with confirmed TB. The pediatric WHO symptom screen was 100% sensitive, but had 4.3% specificity, because of the high prevalence of fever, cough, and poor weight gain in this population. Report of weight loss had better diagnostic performance [AUC .76 (95%CI .66-.86)] than the pediatric WHO TB screen [AUC .52 (95%CI .51-.54)] or any other symptom. A modified pediatric TB symptom screen including weight loss, prolonged fever and cough, and TB contact history had AUC .70 (95%CI .62-.78).

Conclusions: Hospitalized HIV+ children frequently had TB symptoms. The WHO pediatric TB screen had high sensitivity but poor specificity for confirmed TB; use of weight loss instead of poor weight gain may improve clinical algorithms for TB screening in HIV+ children.

OA-376-28 Successfully tested but not enrolled in HIV treatment and care: missed opportunities for TB patients in Papua New Guinea

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Background: The quality of treatment and care for HIV co-infected TB patients may be affected by poor linkages between HIV and TB services. This study aimed to investigate the current situation of linkages between two services in Papua New Guinea (PNG) in order to explore possible strategies to improve the quality of care.

Methods: The patients enrolled for anti-TB treatment at all 15 health centers in the national capital district (NCD) from January to December 2014 were included. All the health centers provided TB services and HIV testing services. While 5 centers provided anti-retroviral therapy (ART) services (ART sites), 10 centers did not provide ART services (non-ART sites). Data on HIV testing, referral to HIV care and ART initiation obtained from TB treatment registers and records were reviewed and analyzed.

Results: Over this period, 6,390 patients (male 53.4%, female 46.6%, median age 25.0 years) had started anti-tuberculosis treatment. Two thousand and three hundred ninety-two (37.4%) were tested for HIV, of which 227 (9.5%) were HIV positive. One hundred thirteen (48.1%) of co-infected patients were referred to HIV services, and of them 86 (36.6%) initiated ART. Detailed analysis on TB-HIV co-infected patients who did not initiate ART showed that 78% of them were lost-to-follow-up (LTFU), 16% were defaulted, 5% were dead and 1% refused ART initiation. In comparison to non-ART sites, ART sites showed significantly lower HIV testing rate among TB patients (27.6% vs. 43.9%, $P < 0.01$) and higher ART initiation rate among TB-HIV co-infected patients (50.0% vs. 32.7%, $P = 0.01$).

Conclusions: This is the first detailed data showing TB-HIV service cascade in the NCD, PNG. HIV testing rate for TB patients still remains low because of weak commitment of healthcare workers on TB-HIV collaborative activities. Additionally enrolment to HIV treatment and care of co-infected patients is another challenge due to poor linkages between two services. In order to capture the apparent high LTFU, the same analysis needs to be done from the HIV databases. Strategic information sharing mechanism between TB and HIV programs urgently required to be established to recognize the gaps in the TB-HIV collaborative activities and proceed onto strategic planning.

OA-377-28 Patient preferences for provision of isoniazid preventive therapy among people living with HIV in South Africa

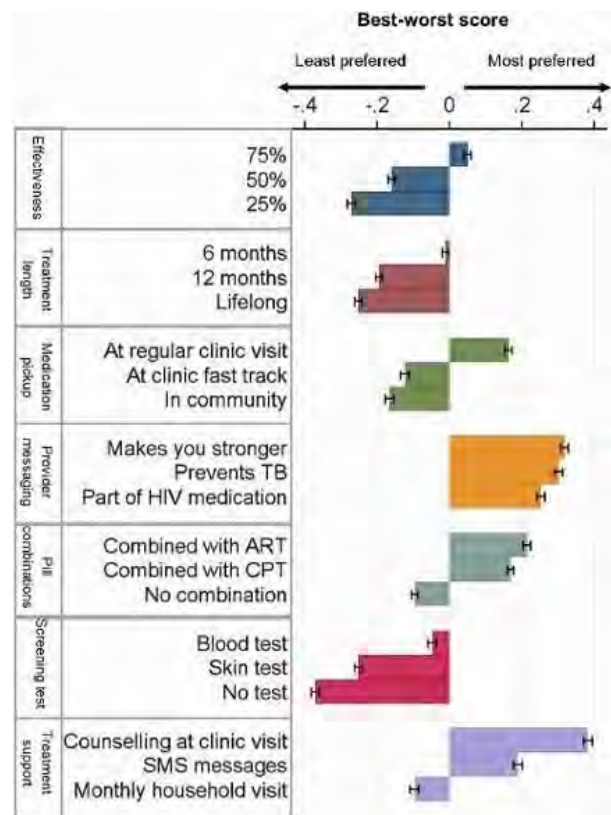
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Background: Implementation of isoniazid preventive therapy (IPT) for TB prevention among HIV-infected individuals remains challenging— < 30% of eligible patients worldwide started IPT in 2013. We aimed to understand patient preferences for IPT in order to develop patient-centered implementation strategies which improve uptake.

Methods: We conducted a cross-sectional survey of adults with recent HIV diagnosis (< 6 months) at 14 primary care clinics in South Africa. Using profile-based best-worst scaling, patient preferences were elicited across 7 attributes of IPT (effectiveness, treatment length, medication pickup location, medication purpose messaging, pill combination with other HIV medications, screening test, treatment support), each across 3 different levels. Best-worst scores, ranging from -1.0 (lowest preference) to 1.0 (highest preference) were calculated as the frequency that each attribute level was chosen as best or worst from a series of options. Relative attribute importance was calculated as the proportion of total variability among attribute levels explained by that attribute (0-100%).

Results: From 2014-2015, we enrolled 334 HIV-infected individuals. Median age was 34 years (IQR 27-41), 64% were women, median time since HIV diagnosis was 28 days (IQR 9-79), 56% were on antiretroviral therapy (ART) and 35% were on IPT. Treatment support had the highest relative importance among those surveyed (23%), while medication pickup location, screening test and pill combinations were of equivalent importance (~15%). Preference was highest for support through clinic-based counselling (0.38 ± 0.01), positive messaging about IPT purpose (range $0.25-0.32$), and combination with ART (0.22 ± 0.01) or cotrimoxazole (0.17 ± 0.01). Community-based interventions such as community IPT pickup (-0.17 ± 0.01) were preferred less relative to clinic-based interventions. Preferences did not vary by sex, CD4 count IPT or ART use.

Conclusions: Preferences for IPT provision among people living with HIV in South Africa suggest several simple low-cost strategies, including positive messaging about the purpose of IPT, clinic-based treatment support, and a combined pill with cotrimoxazole or ART may increase uptake.



OA-378-28 Urgent interventions to improve isoniazid preventive therapy delivery in Swaziland

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Background: In 2011, Swaziland's Ministry of Health endorsed Isoniazid Preventive Therapy (IPT) to treat latent tuberculosis (TB) infection in persons living with HIV (PLWH). However, in 2014, less than 10% of eligible patients received IPT and only 32% of those had documented treatment completion. Since the optimal model for IPT delivery is unknown, we studied IPT delivery models based on patient preference to improve treatment outcomes.

Methods: We conducted a prospective cohort study of patient-selected IPT delivery at five HIV clinics. Trained clinicians offered a convenience sample of eligible PLWH 6-months of IPT through facility-based or community-based delivery (the latter via home-based care or a peer-support group). IPT medication refills were scheduled to coincide with antiretroviral refills. Adherence and treatment completion were documented by pill counts and self-report during clinic visits, home visits and telephone calls.

Results: Between February and August 2015, 909 participants were enrolled and followed through Febru-

ary 2016. Most were female (66%) and the median age was 38 years (1 month-78 years). Nine participants screened positive for TB disease at any visit; all had TB disease excluded by evaluation with chest X-ray and sputum examination and continued in the study. A total of 789 (87.8%) chose facility-based delivery and 111 (12.2%) selected community-based; none selected the peer-support group. Adherence to at least 80% of prescribed doses during the first three months of treatment was documented for 857 (94.3%); adherence rates were similar for both cohorts (98.0% and 94.6% in the facility-based and community-based cohorts respectively, $P > 0.05$). A total of 813 (89.4%) participants completed treatment: 712 (89.2%) in facility-based and 111 (91.0%) in community-based care ($P > 0.05$). No treatment failures occurred. Few participants discontinued IPT (56, 6.2%) or were lost to follow up (37, 4.1%). **Conclusions:** PLWH achieved high rates of IPT adherence and treatment completion through our model of patient-selected IPT delivery coordinated with antiretroviral refills. Symptom screening of patients on IPT did not identify any episodes of TB disease. This delivery model may improve outcomes by simplifying appointment schedules and conferring agency, and may be readily implemented in similar settings with high rates of TB-HIV.

OA-379-28 Modeling the implementation of population-level isoniazid preventive therapy for tuberculosis control in a high HIV prevalence setting

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Background: Isoniazid Preventive Therapy (IPT) for individuals with latent TB infection is standard of care in developed countries, but its use in regions with high HIV burden is limited, in part because the evidence on the efficacy and safety of IPT in high dual-burden contexts is mixed. We model the projected epidemiologic impact of providing IPT to South African adolescents, among whom HIV prevalence is low, latent TB prevalence is high, and school-based programs may enable population-level coverage.

Methods: We simulated a dynamic compartmental simulation model of age-structured HIV and TB co-epidemics in South Africa to study the potential population-level impact of providing IPT to adolescents. For HIV, we use a model that includes infection status, CD4 count, and ART (anti-retroviral therapy) status; TB is modeled by disease state (susceptible, latent, active), diagnosis state, treatment status (DOTS), and IPT status. TB dynamics include slow and rapid disease progression. The benefits of IPT include a return to TB susceptibility (a cure for existing latent infection) among 47% of recipients, and TB activation rate while taking IPT that is 8 times slower than among those not on IPT for HIV-negative individuals and 40 times slower than among those not on IPT for HIV-positive individuals not on

ART. We analyze the effects of continuous IPT coverage among adolescents from 5% (baseline) to 90%.

Results: Our model was calibrated to an adult HIV prevalence of 15%, overall TB incidence of 1055 per 100 000 person-years, and TB mortality of 250 per 100 000 in 2012, consistent with WHO and UNAIDS estimates. At current IPT coverage, we estimate that TB incidence will decline by between 2-12% per year compared to baseline starting in the 7th year. At current IPT cure rates, increasing IPT coverage to 50% among adolescents is expected to reduce TB incidence by years compared to baseline. An increase of IPT to 90% further increased the anticipated benefits.

Conclusions: We demonstrate the potential epidemiological benefits of targeting IPT to a population with high latent TB prevalence and low HIV prevalence, where the possible harms from false-negative diagnosis of active TB are low.

11. Bacteria, vaccines and immunity

OA-380-28 Previous BCG vaccination associated with variation in mycobacterial-specific immune response: a modelling study

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Background: Mathematical modelling could give us mechanistic insight into dynamics of immune response following vaccination and the ability to quantify the differences in these responses attributed to population covariates. We use modelling techniques to investigate the immune response to vaccination with the tuberculosis (TB) vaccine Bacillus Calmette-Guérin (BCG) as a better understanding of the variation in response required to develop a new vaccine against TB disease. We aimed first to develop a model of the immune response dynamics after BCG vaccination in humans, and to calibrate the model to data. Second, we investigated whether population covariates helped reduce variability in predicted model parameters.

Methods: We use IFN- γ as a marker of BCG vaccination immunogenicity and as such, use available ELISPOT data on IFN- γ emitting CD4⁺ T cells over time after vaccination in 55 humans. Human population covariates were: BCG vaccination status (previously BCG vaccinated (BCG:Y) or naïve (BCG:N) at enrolment), time since BCG vaccination (including 'never'), gender and monocyte to lymphocyte cell count ratio. The model was a two-compartmental, ODE model describing the dynamics of CD4⁺ effector and memory T cells incorporating a Gaussian 'delay' model representing the delay in initiation of CD4⁺ responses following vaccination. Nonlinear mixed effects modelling was used to estimate population parameters. The analyses conducted were: 1)

calibrate model to the human data, and 2) assess the impact of human population covariates on immune model parameter values. Bayesian Information Criteria (BIC) alongside graphical results were used to assess fit. **Results:** Preliminary results suggest 1) the immune model with a combined residual error model represented the data well. 2) the covariate BCG status was associated with a significant ($P < 0.05$) difference in immune model parameter values; those in the BCG:Y group showed significant increases in parameters associated with increased baseline and peak of response. All other covariates were non-significantly associated.

Conclusions: This analysis suggests that previous BCG vaccination is associated with durable IFN- γ responses. Vaccine trials may need to stratify by BCG vaccination history. Mathematical modelling has provided mechanistic insight into the variation in immune response dynamics and could be a vital tool to accelerate vaccine development.

OA-381-28 Can BCG prevent *M. tuberculosis* infection in guinea pigs exposed to human cases?

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Background: BCG has traditionally been thought to prevent complications of tuberculosis, but prior to the introduction of IGRAs, there was no way to determine if they prevented infection due to the cross reactivity of BCG with PPD testing. Several observational studies in humans have reported reduced IGRA conversion among contacts of TB cases previously vaccinated with BCG. The natural human-to-guinea pig tuberculosis (TB) transmission model mimics a more realistic mode of *Mtb* transmission. We evaluated BCG vaccine efficacy in guinea pigs exposed to naturally transmitted *Mycobacterium tuberculosis*.

Methods: BCG vaccinated and control guinea pigs were continuously exposed for 24 weeks to exhaust air of a 6-bed tuberculosis inpatient hospital ward in South Africa. Serial tuberculin skin test reactions, BACTEC MGIT and pulmonary pathology were measured to determine infection. In addition, lungs and whole blood from groups of animals were evaluated for flow cytometry and qRT-PCR expression of markers of type I interferons (IFN α , IFN β), inflammation (IL-17, IL-1 β), protection (IL-12, TNF α , IFN γ), and suppression (TGF β , Foxp3, IL-10).

Results: BCG vaccinated and control guinea pigs naturally exposed with susceptible TB strains after 8 weeks of exposure resulted in BCG being protective against infection (0% BCG vaccinated vs. 9% unvaccinated, 4% sham vaccinated) and some control animals developed TB disease. Animals developing active disease

demonstrated either a low or a robust immune expression strength of markers of inflammation and suppression. The strongest correlate of infection was BACTEC MGIT and whole blood CFP10/ESAT6 stimulated expression for IFN γ compared to TST and pathological evaluation. However, subsequent exposure of BCG vaccinated and control guinea pigs to 10 more weeks of MDR- and XDR-TB strains resulted in increased numbers of control and BCG vaccinated animals developing active TB (7% BCG vaccinated, 1% unvaccinated, 7% sham vaccinated).

Conclusions: We conclude that the natural human to guinea pig TB infection model can be used to test for vaccine efficacy and that confounding factors such as strain differences and reinfection may contribute to failed BCG vaccine efficacy in a susceptible host.

OA-382-28 The impact of previous BCG vaccination in enhancing the effectiveness of anti-tuberculosis drugs to control mycobacterial growth ex vivo

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Background: Current effort to effectively control tuberculosis (TB) is hindered by lengthy treatment and the emergence of drug resistance. Combining vaccination with drug therapy will enhance host immune response and improve the effectiveness of current treatment. Bacillus Calmette-Guerin (BCG) remains the only licensed TB vaccine to date. Several pre-clinical animal studies have suggested the benefit of BCG vaccination in adjunct to current treatment. A proof-of-principle study using human samples as well as identification of optimum regimens are needed before such concept can be further advanced. Mycobacterial growth inhibition assay (MGIA) is a functional assay that measures the summative ability of host immune cells to inhibit the growth of mycobacteria ex vivo. There is a recent interest as the assay has been shown to better reflect epidemiological data in distinguishing protection and might be a better correlate of protection following TB vaccination.

Methods: We developed an ex vivo MGIA to assess the ability of isoniazid (INH) and rifampicin (RIF) to inhibit the growth of mycobacteria using peripheral blood mononuclear cell (PBMC) from historically BCG-vaccinated and naïve volunteers ($n=20$, respectively). PBMCs were co-cultured for 4 days with *Mycobacterium bovis* BCG as an immune target in the presence of drugs.

Results: BCG-vaccinated participants were superiorly capable of inhibiting mycobacterial growth ex vivo compared to the naïve ($P < 0.005$). The average time since BCG vaccination in this study was 23.8 years. There was a trend towards lesser inhibition of growth in BCG-vaccinated participants originated from regions closer to the equator. BCG vaccination enhanced the ability of INH to control mycobacterial growth at the drug concentrations of 0.01 and 1 $\mu\text{g/ml}$ ($P < 0.05$). In

the presence of RIF, improved drug killing by vaccination was observed at the concentration of 0.01 µg/ml ($P < 0.005$). Ex vivo control of mycobacterial growth was not correlated with IFN-gamma response measured with ELISpot ($P > 0.5$).

Conclusions: This study provided evidences regarding the benefit of BCG in enhancing drugs effectiveness ex vivo. Immune mechanisms responsible for such enhanced drug killing remains to be elucidated. Implementation of the assay to screen optimum combinations of drugs and TB vaccine candidates in early phase clinical trials worth further consideration.

OA-383-28 Efficacy of the BCG vaccine on overall causes of mortality in Brazil

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Background: Several studies have shown protective efficacy of BCG vaccine at birth against tuberculosis ranging from 70-86%. Other studies have shown nonspecific effects of BCG, first dose, decreasing in 17% of overall mortality with greatest effects when applied in the neonatal period. The objective of this study was to evaluate the efficacy of the BCG vaccine, first neonatal or infancy dose, in the overall mortality during school age in the cities of Salvador-BA and Manaus-AM, Brazil.

Methods: This was a controlled randomized community trial without placebo, that started in the period 1996-1998, called REVAC-BCG. Public schools in Salvador and Manaus with children aged 7-14 years were randomized to BCG vaccination (second dose). In the control group, children who had were not vaccinated at birth remained unvaccinated. In the intervention group children not vaccinated at birth received their first dose at school age. Records made up a database with 354 406 children. Probabilistic record linkage was performed Using RecLink III with all deaths recorded to the Information System of Mortality occurred in the both capitals between 1997 and 2014. Descriptive statistics was made to comparison between groups. Mortality rate, Mortality rate ratio and Vaccine Efficacy was estimated by logistic regression with Generalized Estimating Equation (GEE), and survival analysis by Kaplan-Meier. **Results:** A similar and no statistical significant distribution of variables (sex, age and socioeconomic status) was observed in both intervention ($n = 1828$) and control ($n = 1649$) groups in deaths of children who received first neonatal dose, and in both intervention ($n = 62$) and control ($n = 61$) groups in deaths of children who received first dose on infancy. It shows similar risks to death independently of these variables. BCG vaccine was protective against all mortality cause from age 7 onwards as a neonatal dose: 25% (OR 0.75, 95%CI 0.57-1.00), a school age first dose: 10% (OR 0.90, 95%CI 0.63-1.29).

Conclusions: This is the first study in Brazil to evaluate the effect of vaccine on mortality, and the results are consistent with neonatal BCG vaccine being effective in the reduction of overall mortality during adolescence. Others studies must be conducted to better understand and explain how BCG vaccine is involved on this reduction of mortality.

OA-384-28 Delayed-type hypersensitivity response in Balb/C mice vaccinated with chimera DNA vaccine against tuberculosis and leishmania co-infection

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Background: *Mycobacterium tuberculosis* and *Leishmania donovani* are considered to be most deleterious intracellular human pathogens. It has been shown that immunosuppressive conditions caused by *M. tuberculosis* infection may lead to progression of latent *Leishmania* infection to clinical Leishmaniasis. Approximately 20% cases of tuberculosis infection are also reported with *Leishmania* co-infection. Thus there is an urgent need to develop dual protective vaccine against *Mycobacterium tuberculosis* co-infection.

Methods: Balb/c mice (6-8W) were immunized *L. donovani* with 5 different plasmid constructs; Chimera vaccine (Esat-6+Kinesin), *Leishmania* specific kinesin, *M. tuberculosis* specific Esat-6, Empty pVAX plasmid, and Saline as a control. After booster dose, footpad swellings were measured (in *M. tuberculosis*, *L. donovani* and *M. tuberculosis* + *L. donovani* co-infected groups) at 24 and 48 hrs.

Results: *M. tuberculosis* + *L. donovani* infected group: Average DTH response in ESAT-6 was slightly higher (0.32 mm) than chimera (0.3 mm) and kinesin (0.23 mm) vaccinated mice in comparison with the pVAX (0.19 mm) and Saline (0.14 mm) vaccinated mice at 24hrs; whereas DTH response at 48hrs in comparison with saline (0.18 mm) and pVAX (0.2 mm), the ESAT-6 (0.38 mm), Kinesin (0.28 mm) and chimera (0.39 mm) had higher values. The response at 48 hrs was similar with little higher DTH value than at 24 hrs. There was no significant increment in DTH response at the difference of 24 hrs in the TB infected group. *L. donovani* infected group: At 24 hrs, the average DTH response was higher in chimera (0.37 mm), than Kinesin (0.32 mm) and ESAT-6 (0.29 mm) where as the response shown at 48 hrs was higher in kinesin (0.42 mm) than chimera (0.41 mm). DTH response of ESAT-6, pVAX and saline at 24 hrs and 48 hrs were 0.29, 0.20 and 0.12, and 0.35, 0.27 and 0.16mm, respectively. *M. tuberculosis* infected group: Average DTH response in ESAT-6 (0.30 mm) was higher than the chimera (0.29 mm), Kinesin (0.21 mm), as compared to empty plasmid (0.20 mm) and saline (0.11 mm) at 24 hrs. While DTH response was higher in ESAT-6 (0.39 mm) than chimera (0.38 mm),

kinesin (0.27 mm), as compared to the plasmid (0.26 mm) and Saline (0.17 mm) as a control.

Conclusions: Chimeric vaccine construct could induce cellular immune response against both pathogens. Moreover, immune response generated by chimeric construct was found superior to that of individual vaccine constructs, suggested an adjuvant affect of these antigens over each other. Thus Chimeric DNA vaccine could be a potent immunoprotective candidate for tuberculosis and leishmaniasis co-infection.

OA-385-28 *Mycobacterium tuberculosis*-specific interferon-gamma responses, the Beijing-lineage, and plasma adipocytokine levels in patients with active tuberculosis

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Background: Recent studies suggest that *Mycobacterium tuberculosis* lineages may affect host immune and inflammatory responses differently, and that these responses are associated with adipocytokine levels in part. We investigated whether *M. tuberculosis*-specific interferon (IFN)-gamma responses and adipocytokine levels are affected differently by *M. tuberculosis* lineages/sublineages in patients with tuberculosis (TB) before and during the treatment course.

Methods: Interferon-gamma release assays (IGRAs) were performed for 489 patients with newly diagnosed pulmonary TB at three points of time: month 0 before anti-TB treatment, and months 2 and 7 after starting treatment. *M. tuberculosis* strains isolated from the patients were classified into non-Beijing, ancient-Beijing and modern-Beijing sublineages using the PCR-based typing methods. Levels of adiponectin and leptin in the plasma supernatants that remained after performing IGRAs were also measured using enzyme-linked immunosorbent assays in 46 patients of the same cohort. Random coefficient models were used to compare longitudinal patterns of IFN-gamma responses and adipocytokine levels among the groups.

Results: Before treatment, the IFN-gamma responses were highest in the ancient-Beijing patient group, followed by the modern-Beijing and non-Beijing group, even after adjustment for age, gender, and other confounders (adjusted means = 7.69, 6.36 and 5.21 IU/ml respectively; $P = 0.0201$). During treatment, the IFN-gamma responses were decreased in the three groups, but slightly increased between month 2 and month 7 in the modern-Beijing group. The time-dependent response patterns were significantly different among them by the

post estimation test ($P = 0.0305$). Before treatment, the modern-Beijing group, but not ancient-Beijing group, affected elevation of adiponectin levels significantly, when non-Beijing group was set as reference, even after adjustment for body mass index, age and sex ($P = 0.033$). During treatment, adiponectin levels increased further at month 2 and then decreased in all of the groups, but the patterns of time-dependent changes were significantly different among them ($P = 0.0125$). Leptin levels were increased or not changed at month 2 and the patterns of time-dependent changes were not different among them. **Conclusions:** Our data suggest that the Beijing lineages/sublineages have different effects on immune and inflammatory responses. Further investigation on the underlying mechanisms and possible interventions are desired.

OA-386-28 First comparative proteomic analysis of the *Mycobacterium tuberculosis* lineage 7

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Background: A new phylogenetic *Mycobacterium tuberculosis* lineage termed lineage 7 has been identified in Ethiopia. A recent study demonstrated that lineage 7 is associated with prolonged clinical delay among patients and grows slowly in vitro compared to other lineages. Given the potential implications for pathogenesis and virulence of mycobacteria, proteomic studies of *M. tuberculosis* are warranted. The aim of this study was to delineate the proteomic profile of *M. tuberculosis* lineage 7 relevant for its growth and pathogenesis.

Methods: We used a label-free quantitative proteomics approach to characterize and compare differences of two *M. tuberculosis* lineages (lineage 7 and lineage 4) at the level of global protein expression. Three biological replicates were injected a nano-LC-MS/MS and Q Exactive mass spectrometer (Thermo) in technical triplicates and quantified using a label-free quantitative (LFQ) algorithm. Functional annotation enrichments and identification of protein interaction networks were carried out using Gene Ontology and the Search Tool for the Retrieval of Interacting Genes/Proteins, respectively. **Results:** Global protein expression analysis yielded identification of 2825 and 2541 proteins in lineage 7 and lineage 4, respectively. Among 2825 proteins identified in lineage 7, 2499 (87 %) were shared by all the biological experiments. Likewise, 1966 (77%) proteins were shared by all the biological experiments in the lineage 4. Comparison of LFQ intensities between lineage 7 and lineage 4 showed that 101 proteins were significantly differentially expressed (DE) (t -test $P \leq 0.05$, fold change cutoff ± 1.5). Protein network analysis indicated that the significantly DE proteins belong to nine networks in which five were interconnected to lipid

metabolism and small molecule trafficking. Notably, the top 10 down regulated proteins were mainly involved in antioxidant and catalytic activities that are essential to defend the bacteria against host and environmental oxidants and reductants.

Conclusions: This study generated novel knowledge regarding the DE proteomic profile of *M. tuberculosis* lineage 7 strains, elucidating its relatively slow growth. Further research is essential to understand the phenotypic consequences of the differential expression profile on the lineage 7 life-style.

OA-387-28 Inflammasomal response after ESAT stimulation could help differentiate between active TB and latent TB infection

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Background: Inflammasomes are an important part of innate immune system and are gaining increasing attention in tuberculosis (TB) pathophysiology. Little, however, is known regarding the inflammasomal response after ex-vivo TB antigen stimulation in active TB patients and those with latent TB infection (LTBI).

Methods: We prospectively recruited eight active TB patients and 5 contacts with LTBI. Monocyte was purified from peripheral blood mononuclear cells and differentiated into macrophage. The expression of target genes in macrophages, including MR (mannose receptor), *NLRC4*, *NLRP3* and TNF-alpha was measured by using Quantitative-PCR after 6-hour ex-vivo stimulating with ESAT-6 protein at 1ug/ml. *GAPDH* was used as the house-keeping gene.

Results: The mean mRNA fold-increase in active TB and LTBI was 1.10 ± 0.76 vs. 0.69 ± 0.26 for MR, 0.63 ± 0.43 vs. 0.73 ± 0.18 for *NLRC4*, 2.28 ± 2.23 vs. 0.85 ± 0.38 for *NLRP3* and 45.8 ± 48.7 vs. 24.2 ± 28.9 for TNF-alpha. Five out of eight active TB patients had up-regulated MR expression while none of the 5 LTBI contacts did ($P = 0.075$). Furthermore, three of the eight active TB patients had a two fold increase in *NLRP3* expression while none of the five LTBI patients did ($P = 0.231$).

Conclusions: Our study found that the expression of MR, *NLRP3* and TNF-alpha is up-regulated in active TB patients compared with LTBI contacts after ex-vivo TB antigen stimulation. MR and *NLRP3* gene over-expression may be specific for active TB disease status. The study is currently ongoing and associated cytokine response will also be measured to validate the findings.

13. Enhanced case-finding and contact tracing

OA-388-28 A systematic review of national policies on tuberculosis contact investigations

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Background: The World Health Organization estimates over a third of new tuberculosis (TB) cases went unreported or undiagnosed in 2014. An effective strategy to find and diagnose people with TB is contact investigation, or the evaluation of close contacts of TB patients for TB infection and disease. Policies for contact investigations are determined by individual countries through national guidelines.

Methods: To describe the content and strength of national guidelines for TB contact investigations, we conducted a systematic internet search and contacted TB programs to obtain national guidelines. For the 22 high burden TB countries, which together represent 80% of the global TB burden, we also sought guidelines through contacts within our personal networks if we could not obtain one through the aforementioned methods. We included in our review all guidelines published in English, Spanish, and French; for the 22 high burden TB countries, we included those published in any language. We used a standardized data abstraction form to collect data about recommendations and policies for contact investigation.

Results: Of 216 countries and territories that report case notifications to the WHO, we found a national guideline in English, Spanish, or French for 71 (33%) countries. Of those, all 71 (100%) contained recommendations for the investigation of tuberculosis contacts. For the subset of the 22 high burden TB countries, we found a national guideline for 18 (82%) countries, of which 13 (72%) were in English, Spanish or French. Of these, guidelines for 6 (46%) countries indicated the health system was responsible for seeking out contacts for evaluation, 3 (23%) placed the responsibility on the patient, and 4 (31%) did not indicate who was responsible. Additionally, guidelines for 10 (76%) countries explicitly prioritized young child contacts for evaluation. While all 13 countries (100%) recommended giving preventive therapy to contacts, 12 (92%) indicated preventive therapy only for young children or people living with HIV.

Conclusions: Of the guidelines captured in our search, all included recommendations on TB contact investigation. Young children were a particular group targeted for evaluation and treatment of infection. Further research is needed to investigate whether recommendations asserted in guidelines translate into implemented practices.

OA-389-28 Comparison of patients identified by active case finding against those identified in health centres

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Background: Limited health care access contributes to a large number of tuberculosis (TB) cases being missed and has led to renewed interest in outreach approaches to increase detection. There is an ongoing debate as to whether outreach activities increase absolute case detection and if patients identified in the community are similar to those attending health facilities.

Methods: Two cohorts of adults with cough >2 weeks were recruited from hospitals and households in urban slums in Abuja, Nigeria. Participants provided sputum for smear-microscopy, demographic and clinical information. We compared their differences by recruitment place and smear status (smear-positive and smear-negative) within and between settings.

Results: 1202 (29.5%) of 4070 participants were enrolled from health facilities and 2868 (70.5%) in the community. 209 (17.4%) facility-based and 485 (16.9%) community-based participants had smear-positive TB. Community participants were older (mean 39.4 vs. 34.0 years) and had more frequent and longer duration of symptoms. TB cases in the community were older (mean 36.3 vs. 31.8 years), had longer cough duration (10.3 vs. 6.8 weeks) and weight loss (4.6 vs. 3.6 weeks) than facility-based patients and complained more of fever (87.4% vs. 74.6%), chest pain (89.0% vs. 67.0%), and anorexia (79.5% vs. 55.5%).

Conclusions: Community-based participants have more symptoms and longer duration of illness than patients screened at health facilities. The differences appeared to be due to factors that delayed or prevented the community cohort at large from accessing healthcare. Community-based activities targeted at urban slum populations may identify cases not accessing stationary services.

OA-390-28 Optimizing the efficacy and efficiency of household contact tracing in sub-Saharan Africa

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Background: Active case finding through household contact tracing of tuberculosis cases is rarely performed by National Tuberculosis Programs (NTPs) in low resource, high burden settings. Furthermore, when implemented, the majority of contacts are missed. Methods to increase the efficiency of household contact investigation for programmatic use are needed.

Methods: Two contact investigations, the Kawempe Community Health study (KCH; 1995-2006) and the Community Health Social Network Study (COHSO-NET; 2012-current), were performed in Kampala, Uganda by the same research team. Field workers visited contacts of laboratory diagnosed tuberculosis cases and enrolled those who consented. Subsequently, all contacts were assessed for tuberculosis disease through a physical examination and laboratory diagnostic testing. Risk differences for co-prevalent disease were calculated for contact, index case, and environmental characteristics. We then measured the number of contacts needed to screen (NNS) to detect a case of co-prevalent by several risk factors from the KCH study and evaluated the yield of disease in COHSO-NET by the most influential factor.

Results: In total, 1941 and 951 contacts of tuberculosis cases were enrolled in the KCH and COHSO-NET studies. The number of contacts needed to screen to detect one co-prevalent tuberculosis case was 23.8 (4.2% prevalence) in KCH and 45.5 (2.2% prevalence) in COHSO-NET. In KCH, the variable with the lowest NNS to detect one additional case was current cough of the contact (NNS = 5.1, 95%CI, 4.13-6.81). In KCH, 21% (60/287) of contacts with cough had co-prevalent disease. When we studied contacts with cough in the COHSO-NET cohort of contacts we found that 34.6% (18/52) had co-prevalent disease. In all, screening only contacts with cough detected 77% (60/78) and 90% (18/20) of all co-prevalent cases found in the KCH and COHSO-NET studies, respectively.

Conclusions: These results in a low-income, sub-Saharan African setting suggest that detecting contacts with cough is highly resource efficient and may be a viable method to increase case detection at a programmatic level. Tracing contacts that are currently coughing should be included in current policy recommendations for NTPs in high-burden areas.

OA-391-28 Do pilot active case finding projects increase case notification of sputum smear-positive tuberculosis at national level?

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Background: Active tuberculosis case finding (ACF) projects have mostly described an increase of the notification rate in the area of intervention. The objective of this study is to measure the impact of ACF on the case notification of sputum smear-positive (SS+) TB at the national level.

Methods: Case finding results of the 16 countries which have participated to the first wave of the TB Reach project were analysed. Following the results of TB Reach, we used two methods to achieve our goal. First we described the variation of case notification at the national level and then a segmented linear regression was used to analyse the impact of the TB Reach project on the case notification of SS+ TB at the national level for 2005-2013, before, during and after the intervention.

Results: The TB Reach project described in almost all countries an increase of SS+ TB cases from 3% to 334%. Before, during and after the implementation of the TB Reach project, the variations of case notification at country level were often within the expected range from -10% to +10% for most countries. Using segmented linear regression, before implementation of the ACF project, there was a significant year-to-year change in the case notification of SS+ TB in most countries. During the intervention, there was no impact on case notification at national level in any of the countries, except Benin and Kenya. After intervention, there was a significant decrease in the number of cases notified at national level in some countries.

Conclusions: In general, ACF projects have no influence on the case notification of SS+ TB at national level. Our hypothesis is that the ACF projects are pilot projects and difficult to reproduce at the national level, largely because of the high cost and a lack of human resources.

OA-392-28 Risk factors associated with undetected pulmonary TB in a prevalence survey, Callao, Peru

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Background: Prevalence surveys are an important epidemiological tool to characterize true pulmonary tuberculosis (TB) burden and inform and develop strategies for early detection of TB disease in high-risk groups. We performed a prevalence survey in households previously affected by TB.

Methods: From December 2007 through June 2012, consecutive patients diagnosed with TB by the National Tuberculosis Program were recruited. Written, informed consent was obtained from all patients and socioeconomic and health data collected on behalf of their household. We revisited TB patient's households at least 2 years after the patient began TB treatment. At this visit, we recruited all patients and their household contacts, completed a questionnaire and obtained a sputum sample from all participants aged over 7 years. All sputum samples were processed using a 'single step' technique and cultured on thin layer agar.

Results: 2261 patients were recruited at baseline that had a total of 13 254 household contacts registered at recruitment. Of these, 1711 patients (76%) and 9134 household contacts (69%) were aged over 7 years old and available at follow-up. Sputum samples were collected from 1215 patients (71%) and 5180 household contacts (57%). Overall, 51/6395 (0.8%) had a positive sample (797 pulmonary TB cases per 100 000 population). At the time of the prevalence survey 89/6395 (1.4%) participants were taking TB treatment. Excluding these patients, 47/6306 (0.7%) were culture positive. These people were more likely to have a poorer poverty score (RR = 2.4, $P = 0.02$), be a household contact of a patient with multidrug-resistant TB (RR = 2.9, $P = 0.009$), a history of incarceration (RR = 8.5, $P < 0.001$), and self-reported diabetes (RR = 4.4, $P = 0.01$) (Table).

Conclusions: The prevalence survey identified a significant number of undetected pulmonary TB cases. Further strategies are required to identify a cost effective method of implementing active case finding among people at high-risk of TB who would benefit from sputum examination.

Table Factors associated with undetected pulmonary TB

Characteristic	Culture positive n/N (%)	Culture negative n/N (%)	RR (95% CI)	P value
Poverty score (lowest tertile)	23/47 (49%)	2325/6259 (37%)	2.4 (1.1 - 4.8)	0.02
Known MDR-TB exposure at home	8/30 (27%)	394/3403 (12%)	2.9 (1.3 - 6.6)	0.009
History of incarceration	7/47 (15%)	143/6254 (2.3%)	8.5 (3.4 - 20.1)	<0.001
Diabetes (self-reported)	3/47 (6.4%)	121/6248 (1.9%)	4.4 (1.3 - 14.3)	0.01

OA-393-28 Targeting TB preventive therapy to adult household contacts at high risk using a TB risk score

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Background: Use of tuberculosis preventive therapy (PT) must be urgently scaled up and provided to people at high-risk of developing tuberculosis (TB) disease. In high-burden settings, PT is poorly utilised and rarely offered to adult household contacts. Furthermore, the tests for TB infection used to guide prescription are unreliable for predicting disease, fraught with logistical challenges and unavailable in many settings. In low- and middle-income countries, a TB risk score could be used to prioritise PT for contacts most likely to benefit. We therefore aimed to develop a risk score to predict TB disease among adult household contacts of patients with TB in Callao, Peru.

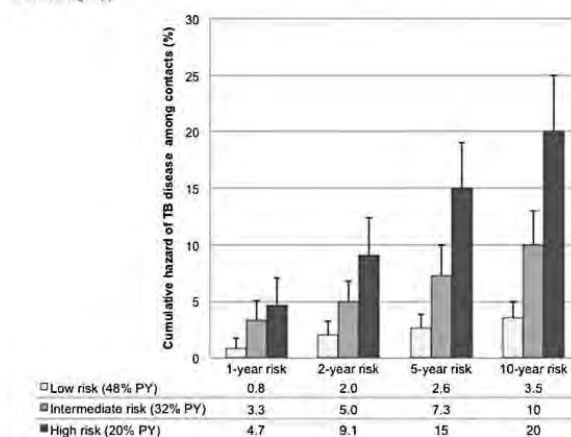
Methods: We identified index-cases with pulmonary TB ($n=715$), recruited their household contacts aged ≥ 15 years ($n=2017$) and followed them for TB for a total of 18 988 person-years (PY). Cox proportional-hazards models were fitted to investigate factors associated with TB. 1009 contacts were selected as a derivation cohort from which a risk score was created. Scores were calculated for each contact and low, intermediate and high-risk groups defined. The score was subsequently validated in the remaining 1008 contacts.

Results: Eight predictors formed the score: age 15-30 or ≥ 50 ; history of TB; body-mass-index; prolonged exposure to the index case; poverty; exposure to indoor air pollution; male index case and high index case smear-positivity. In the derivation cohort the incidence rates in the low-, intermediate- and high-risk groups were 331/100 000PY (95%CI 200-550); 942/100 000PY (95%CI 650-1363) and 2038/100 000PY (95%CI 1501-2768) respectively ($P < 0.0001$). In the validation cohort the rates were similar. The figure shows the cumulative hazard of TB at specific time points. The number-needed-to-treat to prevent one TB case over 2 years in the low, intermediate and high-risk groups is 83, 35 and 18 respectively.

Conclusion: A risk score was derived and validated that stratifies household contacts with different risks of developing TB.

Figure Risk of TB according to risk group

Figure: Histograms showing cumulative hazard of TB among contacts according to risk group using data from the entire cohort. Error bars represent 95% confidence intervals. The data table presents cumulative hazard at 1, 2, 5 and 10 years derived from Nelson-Aalen functions. (% PY=proportion of total number of person years of follow up for each risk group)



OA-394-28 Cost-effectiveness of active case finding of household contacts of pulmonary tuberculosis patients in an endemic setting, Lima, Peru

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Background: We compared the cost-effectiveness of an active case finding (ACF) program for household contacts of tuberculosis (TB) cases enrolled in first-line treatment to the routine passive case finding (PCF) within an established National TB Program in Peru.

Methods: Decision analysis was used to model the incremental costs and effects of four alternate case finding strategies for household contacts. The baseline strategy was a routine TB program where symptomatic cases self-report for evaluation (PCF) and was compared to each of the following: 1) a provider-initiated ACF program; 2) the addition of an Xpert/MTB RIF diagnostic test for a single sputum sample from household contacts, and 3) both strategies combined. Effect estimates of active TB cases detected in ACF and PCF were estimated from published systematic reviews. Direct costs of undertaking household contact evaluations were estimated from an ongoing pragmatic stepped-wedge cluster randomized trial to implement ACF for household contacts of TB cases in 34 healthcare centres in Lima, Peru. Cost-effectiveness analysis was calculated as the incremental cost-effectiveness ratio (ICER) in terms of US dollars per disability adjusted life years (DALYs) averted.

Results: Compared with PCF alone, ACF for household contacts was found to be cost-effective with an ICER of

\$2155 per DALY averted, the addition of the Xpert/MTB RIF diagnostic test resulted in \$ 3275 per DALY averted if implemented in a PCF program, and \$3399 per DALY averted if implemented combined with an ACF program. All strategies remained within the willingness-to-pay threshold for Peru of US \$6360 per DALY averted. In sensitivity analyses, ACF remained cost-effective compared with PCF in scenarios when costs of ACF increased by 4 times (including resources, personnel time and case management costs). ACF using Xpert/MTB RIF for household contacts only remained cost-effective when treatment cure rates remained high for all TB cases detected.

Conclusions: As compared with PCF, ACF of household contacts is highly cost-effective in Peru, including human resource costs to seek out contacts and with an Xpert/MTB RIF diagnostic test. However, ACF including Xpert/MTB RIF was not cost-effective if TB cases detected had poor treatment outcomes, such as when treatment default rates are high.

OA-395-28 Impact of tuberculosis control interventions targeted to previously treated people in a high-burden setting

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Background: Substantial efforts are needed to reach global targets for TB elimination, particularly in high-burden settings. Reaching 90% of high-risk groups through TB control interventions forms part of the global strategy. In Southern Africa, individuals previously treated for TB contribute substantially to the TB burden and might thus be especially attractive for targeted interventions. The purpose of this study was to project the impact of interventions to actively detect and prevent recurrent TB among previously treated people, on TB incidence and mortality in a high-burden setting. **Methods:** We developed a transmission dynamic model of the TB-HIV co-epidemic among individuals with and without a history of TB treatment in a high-incidence community in suburban Cape Town, South Africa. The model was calibrated to local demography, TB prevalence estimates and program data. The interventions modeled were 1) annual active TB case finding (ACF), and 2) lifelong secondary isoniazid preventive therapy (2°IPT) both among individuals who previously completed TB treatment. An average rate of drop-out from 2°IPT of 15% annually was assumed.

Results: We project that a combination of ACF and 2°IPT among 90% of adults with previous complete TB

treatment will lead to a 19.7% reduction in TB incidence and 28.4% reduction in TB mortality at a community level, compared to the projected status-quo 10 years after the introduction of the interventions. Reductions in TB incidence and mortality were highest in the first years after introduction (Figure) and varied with intervention coverage.

Conclusions: Our results suggest that in a high TB burden setting, active case finding and secondary preventive therapy among previously treated individuals could accelerate declines in TB incidence and mortality. Further research is needed to assess the conditions under which these interventions would be cost-effective for TB control in populations highly affected by the disease.

Figure Projections

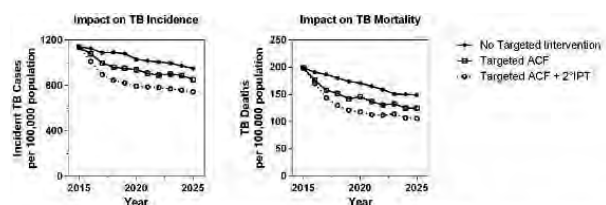


Figure: Projected impact of TB control interventions targeted to adults with a history of previous complete TB treatment on TB incidence and mortality in a high-burden setting in suburban Cape Town, 2016-2026; comparison between the baseline scenario (no targeted intervention) and targeted annual active case finding (ACF) alone and in combination with secondary preventive therapy (2°IPT)

14. Challenges in TB diagnostics: An overview of methods and issues

OA-396-28 Bovine tuberculosis in humans in Germany: what do we know from tuberculosis surveillance?

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Background: The zoonotic potential of *Mycobacterium bovis* was already recognized in Robert Koch's time. However, its importance for human tuberculosis (TB) has been debated. In Germany, bovine TB in cattle was targeted with control programs in the 1950s and by definition bovine TB-free status was reached. As for TB in humans, Germany is a low-incidence country. National TB notification data comprise information on the *M. tuberculosis* complex species and allow us to describe and compare *M. bovis* and *M. tuberculosis* cases in humans.

Methods: We analysed pooled German 2002-2014 TB notification data ($n = 68\,547$) transmitted to the Robert Koch Institute by 1 March 2015.

Results: *M. bovis* was identified in 1.5% ($n = 625$), *M. tuberculosis* in 98.8% ($n = 39\,635$) of all TB cases with bacteriological confirmation and available species information ($n = 40\,531$). The proportion of *M. bovis* cases was stable over time. It ranged from 0.9 to 3.8% across Federal States. Among patients with *M. bovis*, when

compared to patients with *M. tuberculosis*, a higher proportion was female (48% vs. 39%); the median age was higher (71 vs. 47 years) and the country of birth was more often Germany (75% vs. 51%; though not among children < 15 years: 54% vs. 67%). Patients with *M. bovis* presented more often with extrapulmonary TB only than *M. tuberculosis* patients (43% vs. 19%). Pyrazinamide resistance was more frequent (76% vs. 2.0%). Where subspecies information was available (from 2011 onwards), *M. bovis bovis* strains were consistently pyrazinamide resistant (11/11), *M. bovis caprae* strains never (0/5). *M. bovis* cases were less frequently found by contact tracing than *M. tuberculosis* cases (3.7% vs. 12%). Five clusters of epidemiologically linked patients comprised two or more *M. bovis* cases.

Conclusions: Only a small proportion of notified human TB cases in Germany was caused by *M. bovis*. Elderly patients might have been infected at times when *M. bovis* prevalence in cattle was high in Germany. Rare recent transmission cannot entirely be ruled out. Targeted contact tracing efforts compassing humans and animals and use of genotyping/sequencing methods may help to further clarify the role of zoonotic and potential human-to-human *M. bovis* transmission.

OA-397-28 Low-cost automated tuberculosis whole smear screening system

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Background: Computer-aided tuberculosis whole smear screening system consists of real-time focusing, digitally capturing images, and providing diagnostic grading is developed. It can work in both bright field and fluorescence modes. The study was to examine its performance in TB diagnostic algorithms on concentrated smears with AO staining, as well as direct smears with AO and ZN staining, using culture results as the gold standard. The comparison of machine grading and manual smear grading was also given.

Methods: Sputum samples from adult patients with presumed TB for the study were divided into three batches: 1) auramine-stained, 2) Ziehl-Neelsen-stained, and 3) prepared by concentration method and auramine-stained. All slides were graded by experienced microscopists and by the whole smear screening system. We evaluated sensitivities and specificities of TB diagnostics algorithms using our system alone, and in combination with microscopists. Performance was also assessed by the percentage symmetric difference (PSD) between two positive-negative grading results and the major discrepancy rate (MDR) between two 5-level smear grading results.

Results: Of 488 direct smears with AO staining, 228 were culture-positive. Our system gave a sensitivity of 81.6% and a specificity of 74.2%. Of 334 direct smears

with ZN staining, 142 were culture positive. It gave a sensitivity of 70.4% and a specificity of 76.6%. Of 505 concentrated smears with AO staining, 250 were culture positive. It gave a sensitivity of 87.3% and a specificity of 71.0%. To further improve the performance, the machine grading was confirmed by the smear grading when the number of AFBs detected fell in uncertainty ranges (5-15 for AO; 3-13 for ZO). This combined result gave a significant improvement in specificity (AO-direct:85.4%; ZN-direct:92.5%; AO-concentrated:85.4%) and slight improvement in sensitivity (AO-direct:86.0%; ZN-direct:77.5%; AO-concentrated:87.2%) while requiring only limited workload. Low PSD/MDR (AO-direct:16.0%/12.5%; ZN-direct:17.4%/8.4%; AO-concentrated:15.4%/9.7%) were also observed.

Conclusions: The whole smear scanning system achieved high sensitivity without substantially compromising specificity when compared to culture results. Significant improvement in specificity was obtained when machine-graded uncertain results were confirmed by the smear grading. High consistency with smear grading was also observed. This promising approach has potential to reduce significantly the number of slides reviewed by microscopists.

OA-398-28 Serial molecular testing improves the detection of tuberculosis in a low-prevalence setting

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Background: Few data exist regarding the performance of molecular diagnostics for TB in low prevalence settings such as the USA. In 2014, the Los Angeles County Public Health Laboratory began to offer a laboratory-developed IS6110 real-time polymerase chain reaction (PCR) assay for evaluations of pulmonary TB in outpatient public health clinics.

Methods: Data were examined for sputum specimens collected from patients during 2014-2015. During the study period, clinic providers were instructed to routinely order three PCR tests per patient with suspected pulmonary TB. A per-specimen analysis included all specimens with a PCR result, AFB smear result, and *Mycobacterium tuberculosis* culture result available. A per-patient analysis included patients for whom at least one PCR result was available. Test sensitivities were calculated with *M. tuberculosis* culture as the gold standard.

Results: During the study period, there were 7079 sputum specimens collected for PCR testing; 675 specimens (9.5%) were *M. tuberculosis* culture-positive and 429 were AFB smear positive. Among specimens that were culture-positive/smear-positive, PCR had a sensi-

tivity of 98.1%. Among specimens that were culture-positive/smear-negative, PCR had a sensitivity of 50.0% (43.6-56.4); sensitivity varied by time to culture positivity quartiles (slowest growing quartile 44.3%, fastest growing quartile 65.0%). Of 2,891 patients with a least one PCR result, 360 (12.5%) had a least one positive *M. tuberculosis* culture result. Among 246 patients with smear-positive TB, the sensitivities for the first, second, and third PCR tests were 85.7%, 96.7%, and 97.9%, respectively. When performed on smear-positive specimens, the serial sensitivities for the first and second PCR tests were 96.4% and 100%. Among patients with smear-negative TB, the sensitivity of serial PCR tests were 24.8%, 40.0%, and 52.4% for the first, second, and third sputum specimens.

Conclusions: In an outpatient public health setting in the USA, PCR displayed substantial improvement in diagnostic sensitivity when compared to AFB smear microscopy. Performing a second or third PCR test on additional specimens further improved diagnostic yield for patients with either smear-negative or smear-positive TB, and depending on costs, could be considered as a routine practice in low prevalence settings.

OA-399-28 Diagnosing extra-pulmonary tuberculosis by Xpert® MTB/RIF: the Bangladesh experience

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Background and challenges to implementation: Diagnosis of extra-pulmonary TB is often difficult to establish, since the number of bacteria in extra-pulmonary specimens is often lower than the number in pulmonary specimens. Conventional microscopy could not detect AFB in majority of the extra pulmonary lesion. On the other hand cytohistology and tuberculin test are all non-bacteriological evidence as well as not sensitive and specific. So there is a need for simple low cost sensitive and specific test for bacteriological evidence for EPTB.

Intervention or response: The study was carried out at National Tuberculosis Reference Laboratory (NTRL), National Institute of Diseases of Chest and Hospital (NIDCH), Bangladesh. Samples were collected from all the patients with different extra-pulmonary lesion attended in the NTRL. Xpert MTB/RIF assay was performed as per the standard. Data from January 2015 to June 2015 were collected and analyzed.

Results and lessons learnt: In total, 295 specimens were tested from January 2015 to June 2015 which comprised 59 lymph node, 56 pus, 21 urine, 24 tissue, 35 pleural fluid, 84 broncho alveolar lavage (BAL), 15 cerebro spinal fluid (CSF) specimens. From 59 lymph node specimens, 26 (44%) cases were found as *M. tuberculosis* positive including 2 RIF resistant. 30(53.57%) cases were found as MTB positive from 56 samples of Pus, 13(54%) cases were found as *M. tuberculosis* positive from 24 tissue samples, 5(14.28%) *M. tuberculosis* positive including 1

RIF resistant cases found from 35 pleural fluid samples, 21(25%) *M. tuberculosis* positive cases from 84 BAL samples, 2 (13%) *M. tuberculosis* positive cases were found from CSF but no *M. tuberculosis* positive case were found from urine specimen. Overall, 99 (33.37%) of the 295 specimens were identified as *M. tuberculosis* positive by GeneXpert MTB/RIF.

Conclusions and key recommendations: Nevertheless from our results, one can conclude that the Xpert assay is showing can be applied to extra-pulmonary specimens with a high yielding rate which coupled with its speed and simplicity, make this technique a very useful tool for the diagnosis of extra pulmonary tuberculosis.

OA-400-28 A systematic review of the diagnostic accuracy of TB-LAMP for pulmonary tuberculosis

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Background: TB-LAMP (Eiken, Tokyo, Japan) is being explored as a rapid, point-of-care diagnostic test in resource-limited settings. As part of the World Health Organization's guideline development process, we conducted a systematic review of published and unpublished TB-LAMP studies to assess the performance of TB-LAMP as a diagnostic test for pulmonary TB.

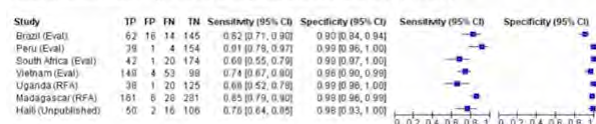
Methods: Four PICO-style questions were developed to assess TB-LAMP performance as compared with smear microscopy and GeneXpert using individual-level data from all studies of TB-LAMP that met eligibility criteria conducted between Jan 2012 and September 2015. Study quality was evaluated using the QUADAS-2 tool. Participants' TB status was classified based on 3 culture-based reference standards of varying stringency. Pooled sensitivity and specificity estimates and differences were obtained using bivariate or random effects meta-analysis, as appropriate.

Results: 4760 adults across 13 studies were included, of whom 10% were HIV-infected (all from 4 studies). The quality of evidence was rated as low for all studies, in part because mycobacterial culture was performed inadequately. TB-LAMP had a pooled sensitivity of 77.7% (95%CI 71.2-83.0) and pooled specificity of 98.1% (95%CI 95.7-99.2). TB-LAMP was more sensitive than smear microscopy (pooled sensitivity difference +7.1% [95%CI 1.4-12.9] to +13.2% [95%CI 4.5-21.9]) and as specific (pooled specificity difference -1.8% [95%CI -3.8 to +0.2] to -1.3% [-3.1% to +0.4]). Compared to Xpert MTB/RIF, TB-LAMP was less sensitive (pooled sensitivity difference -6.9% [95%CI -12.8 to -1.0]) to -2.5% [95%CI -8.0 to +2.9]) and as specific (pooled specificity difference 0.5% [95%CI -0.9 to +1.8] to 1.1% [-0.7 to +2.8]). The pooled proportion

of TB-LAMP indeterminate/invalid results was low (0%, 95%CI 0-0).

Conclusions: TB-LAMP is more sensitive than sputum smear microscopy but likely less sensitive than Xpert MTB/Rif. The specificity of all three tests is similar. TB-LAMP should be considered as a replacement test for sputum smear microscopy in settings where Xpert MTB/RIF is not feasible due to resource and/or infrastructure requirements.

Figure 1. The figure shows forest plots of TB-LAMP sensitivity and specificity standards for individual studies using reference standard 1. Patients were classified patients as having TB if ≥ 1 positive culture was confirmed as *M. tuberculosis* by speciation testing. To be classified as not having TB, patients were required to have no positive and at least 1) two negative cultures on two different sputum specimens (Standard 1). Heterogeneity was significant for both sensitivity (Standard 1: I^2 72%, $p=0.002$) and specificity (Standard 1: I^2 61%, $p=0.02$). Pooled sensitivity was 77.7 (71.2-83.0) while pooled specificity was 98.1 (95.7-99.2).



OA-401-28 Misclassification of tuberculosis as other lung diseases in a tertiary chest disease hospital of a high prevalence country

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Setting: National Tuberculosis Reference Laboratory (NTRL) at National Institute of Diseases of the Chest and Hospital (NIDCH), Bangladesh.

Background: NTRL, NIDCH is the central laboratory of NTP, Bangladesh responsible for the diagnosis of tuberculosis (TB) and drug resistance (DR-TB). NIDCH is the only tertiary chest disease hospital in Bangladesh treating patients of both TB and other lung diseases. Due to overlapping of symptoms, TB are DR-TB cases are misclassified as other lung diseases. This is one of the barriers of TB control.

Objective: To detect TB/DR-TB cases from provisionally admitted other lung diseases with or without previous TB history.

Methods: Early morning sputum was collected from 476 consecutive admitted patients having provisional diagnosis of other lung diseases during April to September 2015. It was tested parallel with LED fluorescence microscopy, culture and DST by NALC-NAOH method & GeneXpert MTB/RIF from the rest of the sediment.

Results: Among 476 admitted cases, 114 (24%) had a previous TB history and 362 (76%) had no previous TB history. Through GeneXpert MTB/RIF, a total of 59 (12.39%) *Mycobacterium tuberculosis* cases were detected, of which 4 (6.78%) were rifampicin resistant. Among these, 26 (22.8%) and 33 (9.1%) *M. tuberculosis* cases respectively were detected in each group. Two rifampicin resistant TB cases (7.7%, 2 of 26 & 6.1%, 2 of 33 respectively) were also detected in each group. The microscopy was positive in 16 & 20 cases, respectively. Among the 59 Xpert positive cases, 56 were positive by

culture. Additionally 2 were added from the Xpert negative group. Through DST, 4 rifampicin resistant -TB case were confirmed as MDR.

Conclusions: The above results indicate that due to overlapping of symptoms, a good proportion of TB & DR-TB cases remain undiagnosed due to misclassification of diseases even in a tertiary level hospital. Rapid screening by GeneXpert MTB/RIF may detect these hidden cases.

OA-402-28 Missed opportunities for rapid diagnosis of rifampicin-resistant tuberculosis in the setting of universal Xpert® MTB/RIF coverage in South Africa

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Background: GeneXpert® MTB/RIF (GXP) is a rapid diagnostic tool which detects both tuberculosis and rifampicin-resistance (RR). South Africa rolled out GXP as the primary TB diagnostic tool in 2012. We assessed the proportion of RR-TB cases diagnosed with GXP and describe missed opportunities to potentially provide earlier diagnosis of RR-TB in Khayelitsha, South Africa.

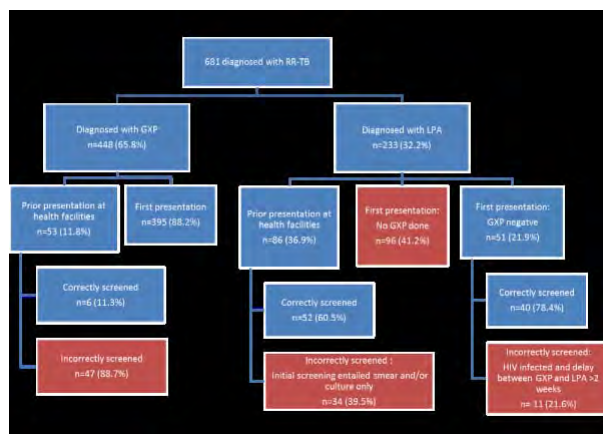
Methods: We conducted a retrospective cohort analysis to ascertain patient diagnostic pathways for RR-TB from January 2012 through December 2014. To identify opportunities where RR-TB may have been diagnosed earlier, routine programmatic and laboratory data were linked. Patients who underwent TB testing in the 6 months prior to RR-TB diagnosis date (specimen date) were considered to have missed opportunities for earlier diagnosis if they were incorrectly screened according to the standard diagnostic algorithm: first specimen was not tested using GXP, or GXP negative result and no subsequent specimen sent for culture and/or drug susceptibility testing (DST) in HIV-infected patients. Patients diagnosed with a test other than GXP, who were not first tested with GXP, were considered to have a missed opportunity for earlier diagnosis.

Results: Among 681 RR-TB patients, 448 (66%) were diagnosed with GXP; the remainder were diagnosed using a line probe assay (LPA, Hain Lifesciences) primarily after culture. Overall, 493 (72%) patients were HIV-infected. In total there were 188 (28%) patients with missed opportunities for an earlier RR-TB result. Of those diagnosed with LPA, 96/233 (41%) never had a GXP conducted an additional 11/51 (22%) patients had delays of >2 weeks between a GXP negative result and submitting a further specimen for testing. There were 53 and 86 patients diagnosed with GXP and LPA respectively, with initial presentation in the 6 months preceding diagnosis, of which 47/53 (89%) and 34/86 (40%) were incorrectly screened.

Conclusions: Earlier RR-TB diagnosis can improve patient outcomes and reduce continuing community

transmission. These data show a high proportion of eligible patients not being tested with GXP and a high proportion of diagnosed RR-TB patients with the potential to have been diagnosed earlier. Further training and monitoring is required if we are to ensure the greatest benefit from GXP implementation.

Figure Diagnosis of RR-TB in Khayelitsha, 2012-2014



OA-403-28 Is introducing the Xpert® MTB/RIF test into the diagnostic algorithm of smear-negative tuberculosis cost-effective?

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Background: Diagnosis of smear-negative pulmonary tuberculosis (PTB) remains a challenge in resource-limited countries. The GeneXpert MTB/RIF (Xpert) assay has shown good performance but the cost of using this test largely has been questioned. We assessed the cost-effectiveness of introducing Xpert assay into the diagnostic algorithm of smear-negative patients with suspicion of TB in Kenya.

Methods: Four PTB diagnostic algorithms were compared: clinical-radiological; clinical-radiological-Xpert; clinical-radiological-culture and clinical-radiological-Xpert-culture. Effectiveness outcomes (culture confirmed TB cases started on treatment) were obtained from two prospective studies of smear-negative patients with suspicion of PTB conducted in 2009-2011 ($n=380$) and 2012-2014 ($n=487$) conducted in the same hospital. Costs were calculated using a 'micro-costing' method. The value of the resources was then estimated from the relevant quantities and corresponding unit price. A discount rate of 4% was applied for both costs and outcomes. Costs and effectiveness of each diagnostic algorithm were compared with the clinical-radiological

algorithm and incremental cost-effectiveness ratios (ICER) were estimated.

Results: The mean costs per patient screened were €29.0 and €49.5 through the clinical-radiological and the clinical-radiological-Xpert algorithms, respectively. The mean cost increased to €72.5 and €90.0 when culture was included in each of them. The cost per confirmed TB case started on treatment was €709 and €753 with the clinical-radiological and the clinical-radiological-Xpert algorithms respectively; and €861 and €1184 when culture was included in each of them. The ICER showed that the cost per one additional patient diagnosed was €825 when the Xpert MTB/RIF assay was added to the clinical-radiological algorithm, €1,320 when culture was added, and €1,743 when both Xpert and culture were added to the clinical-radiological algorithm (Table). **Conclusion:** Introducing GeneXpert test into the clinical-radiological algorithm to diagnose smear-negative pulmonary TB was highly cost-effective (ICER less than two-fold the gross national income), and its adoption could be affordable. Including GeneXpert and culture in the algorithm represented a high cost per additional patient diagnosed and was not cost-effective.

Table CER analysis and ICER (Euros, 4% discount rate)

Algorithms (P) (487 patients)	Costs Euros (C)	Screened and treated cases (E)	Cost-effectiveness ratio	Incremental cost-effectiveness ratio
Clinical-radiological algorithm	14 199	20	709.9 €	
Clinical-radio-Xpert algorithm	24 097	32	753.0 €	825
Clinical-radio-culture algorithm	35 322	36	860.8 €	1 320
Clinical-radio-Xpert-culture algorithm	43 822	37	1 184.4 €	1 743

OA-404-28 Systematic review and meta-analysis of clinical outcomes of drug-susceptible tuberculosis diagnosed by Xpert® MTB/RIF and smear microscopy

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Background: After endorsement by the World Health Organization (WHO) in 2010, over 116 countries implemented the Xpert MTB/RIF (Xpert) assay by December 2014. Published results indicate Xpert has a higher sensitivity compared to smear microscopy for tuberculosis (TB) diagnosis and shorter turnaround times, thus Xpert has the potential to reduce delays in initiation of TB treatment and improve outcomes. We reviewed and evaluated published literature comparing TB treatment outcomes of patients with drug sensitive

pulmonary TB diagnosed by Xpert to those diagnosed by smear microscopy.

Methods: We conducted a systematic review and meta-analysis of all studies reporting TB treatment outcomes according to WHO guidelines among patients diagnosed by Xpert compared to those diagnosed by smear microscopy. A detailed search of the literature up to December 2015 was conducted using MEDLINE, EMBASE, published conference abstracts from the International Union Against Tuberculosis and Lung Disease and lists of references from published articles. Treatment outcomes were categorized as favorable (cured and completed) and unfavorable (failure, death, or lost to follow-up [default]), and were pooled for analysis. To evaluate variation among studies we calculated I^2 to measure heterogeneity.

Result: Publications from four clinical trials (one each from Botswana and Brazil, two from South Africa) met the inclusion criteria. The pooled analysis included patients diagnosed by Xpert (2781) and smear microscopy (2132) who were initiated on anti-tuberculosis treatment and had a known treatment outcome. Among these, 81% (2134/2781) and 78% (1662/2132) reported favorable outcomes, for Xpert and smear microscopy diagnosis, respectively, for a relative risk (RR) of 1.02 (95% confidence interval, 0.99-1.05). Statistical heterogeneity was low among the studies ($I^2 = 0.0\%$, $P = 0.72$). Factors associated with unfavorable outcome, such as time to TB treatment initiation, HIV status and CD4 count, among TB patients diagnosed using Xpert compared to smear microscopy will be discussed.

Conclusions: Our preliminary meta-analysis showed no difference in clinical outcomes for patients diagnosed by Xpert, compared to smear microscopy. Further investigation is needed to address factors associated with unfavorable outcomes in settings with access to Xpert diagnostics.

Table Studies included in the meta-analysis

	Favorable Xpert group	Unfavorable Xpert group	Favorable smear microscopy group	Unfavorable smear microscopy group
Fielding et al, 2015, South Africa	218	31	188	25
Agizew et al 2015, Botswana	130	32	31	8
Trajman et al, 2015, Brazil	1571	444	1267	409
Cox et al, 2014, South Africa	215	34	176	28

15. Tobacco packaging and graphic health warnings

OA-405-28 Tobacco pack warnings in South-East Asia. Where are we after 12 years of the FCTC?

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Background: Tobacco use is a major public health challenge in the South-East Asia Region. Currently, it is responsible for 1.2 million deaths in the region out of the total global mortality of 5.4 million annually. Article 11 of the WHO Framework Convention on Tobacco Control (FCTC) mandates that countries should enact effective measures to ensure appropriate health warnings on tobacco product packages. The Conference of Parties (COP) also adopted guidelines for implementation of this Article. However, existing tobacco health warnings in many countries of the region are yet to fully comply with these recommendations. This paper assesses the status of tobacco pack warnings in the region, challenges encountered to comply with FCTC norms including enforcement, tobacco control stakeholder's response in last 12 years, and lessons learned.

Method: The status of pack warnings, the journey traversed since 2004, tobacco control stakeholders efforts, and tobacco industry and its front groups interference was assessed through e-mails; various reports like Findings from the Cigarette Package Health Warnings: International Status Report, Canadian Cancer Society, Tobacco Atlas, WHO reports; tobacco control review reports and news stories from these countries.

Results: Despite political commitment exhibited by countries in the region, only 2 out of 11 countries have health warnings consistent with FCTC/MPOWER and tobacco products in 4 out of 11 countries do not have any graphical warnings as recommended by it. Nepal is leading in the region with 90% coverage of principal display areas followed by Thailand with 85%. Tobacco industry and its front groups fought forcefully, and lobbied at all levels via political, media, tobacco farmers, manufacturer, traders and vendors. Tobacco Control stakeholders with all their might have very limited success.

Conclusion: The tobacco industry continues to divert attention from the deadly effects of its products through advertising and promotional campaigns, including use of carefully crafted package designs. The tobacco industry tries to undermine the initiatives for effective tobacco control, and this includes attempts to weaken government efforts at introducing pictorial health warnings. Legal measures on tobacco health warnings should be reviewed periodically and updated as new evidence emerges and as specific health warnings and messages wear out with time.

OA-406-28 Changes in Viet Nameese male smokers' reactions towards pictorial cigarette pack warnings over time

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Background: Printing of pictorial health warnings (PHWs) on cigarette packages were obliged by Viet Nam Law on Prevention and Control of tobacco harms since May 2013. Literatures from high-income countries suggest that PHWs motivate smokers to quit smoking though its long-term effect is a question due to wear-out of the PHWs with time. This study aims to assess the changes in salience of PHWs and smokers' reaction towards PHWs over time.

Methods: In May 2014 and May 2015, a cross-sectional questionnaire-based household survey was administered to 1462 and 1509 Vietnamese male smokers aged 18 to 35 respectively. Dependent variable was the respondents' self-reported intention to stop smoking. Main measures were 'Salience of the PHWs', 'Avoidant behaviors', and 'Selection of pack with and without PHW'.

Results: The results showed that compare to wave 1, more smokers in wave 2 noticed and read the PHW. In other word, salience of the PHWs 2 years after the implementation was higher than at the point of 1 year after the implementation. Besides, proportion of smokers who tried to avoid the PHWs reduced from 35% in wave 1 to 23% in wave 2. However, 'Tried to avoid looking/thinking about the PHWs' increased 1.5 times the odds of presenting quit intention compared to those smokers who did not try to avoid the PHWs (adjusted OR = 1.5; 95%CI 1.2-2.0). When time passed by, smokers became less willing to buy the cigarette pack without PHWs if it is not available at the time of buying or is more expensive compared with cigarette pack that have PHWs.

Conclusions: Avoidance regarding PHWs may not work as a barrier when aiming at higher level of quit intention. Salience of the PHWs may increase in the period shortly after their introduction onto packs but would decrease by time. In other words, it would be optimal to change or renew PHWs after a period of implementing to maintain its effects. Alternatives to be considered are to use larger PHWs or plain packaging.

OA-407-28 Overcoming resistance to bigger and better GHWs: case studies from Nepal, Cambodia and Pakistan

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Background: There are an estimated 1.2 billion regular smokers in the world today. Globally tobacco use kills around 6 million people a year; nearly 80% of these deaths are in low- and middle-income countries

(LMICs). Large, hard hitting, graphic health warnings (GHWs) are integral to MPOWER package and critical for reaching out to smokers with low literacy. GHW is one of the most aggressively challenged strategies by tobacco industry (TI). Recently countries like Nepal, India, Sri Lanka, Pakistan, Myanmar and Bangladesh have all pushed for enhanced GHWs, aiming to cover 75% or more of the packs.

Methods: National Health Ministries of these countries faced tremendous pressure by the industry to withdraw their legislations. Misleading arguments about loss of revenue, increased smuggling, collapse of local industry, unemployment of workers and eventually threats of costly litigation were used. The ministries responded by well researched counter arguments to negate the pressure. Civil society organizations and International partners supported the ministries and were instrumental in the success.

Results: Nepal and Cambodia were successful in implementing enhanced GHWs while Pakistan is still struggling. In Nepal, the TI influence over policy makers was rampant. TI attempts were to reduce the size of GHWs from 90% to 75% and delay the implementation; however, they were successfully countered. In Cambodia, TI made a massive effort to block the pictorial health warning regulation; keeping either a 30% text warning or a 30% PHW with text on one side of the pack. However, with strong commitment of the Ministry of Health, and strategic support of The Union, a regulation with 55% PHW was adopted. In Pakistan the case is in High Court and faces a long, expensive judicial process. **Conclusions:** Firm commitment to public health by Health ministries, strong civil society presence and The Union's strategic partnership with government were the key success factors. Media played a vital role by providing facts and figures to the policy makers, public and even to the High/Supreme court.

OA-409-28 Are health warnings really effective?

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Background: Large, hard hitting, pictorial health warnings (PHW) are a central part of the MPOWER package and are especially relevant in low and middle income countries where a large segment of the population is not literate and hence textual warnings have little to no impact. Article 11 of the WHO Framework Convention on Tobacco Control (WHO FCTC) requires parties to the Convention to implement large, rotating health warnings on all tobacco packaging and labelling. Experiences from across the globe will be shared to illustrate the effectiveness of PHW.

Methods: In 2015, a cross-sectional survey was conducted using a semi-structured questionnaire among 5355 (current smokers 1901) participants in Indonesia and 2250 (670 current smokers) participants in Nepal.

Participants were randomly selected from 18 cities in Indonesia and 9 cities in Nepal. Direct interviews were made by trained interviewers. Descriptive and analytical analysis was made. Ethical clearances were obtained from Airlangga University in Indonesia and Nepal Health Research Council in Nepal. Informed consent was received from the participants.

Results: PHW on cigarette pack in the last 30 days was seen by the 93.8% participants in Nepal and 94.3% in Indonesia. About 90% of the participants in both countries found PHW were popular. Of the current smokers (CS), 70.8% in Indonesia and 82.1% in Nepal viewed that PHWs are effective in building awareness on danger of tobacco use. About 47% of the CS in Indonesia and 58% in Nepal told that PHW made them think to quit smoking. PHW made the smokers to reduce cigarettes smoked/day (in Indonesia 27% reduction; from 15 to 11 cigarettes/day, in Nepal 55% reduction; from 11 to 5 cigarettes/day) in both countries. There was a larger impact in Nepal due to the fact that Nepal has a larger 75% PHW on cigarette pack compared to a 40% PHW in Indonesia. More than 90% of the youth in both countries expressed PHW would be effective discouraging youth to start smoking.

Conclusions: The findings suggest that PHWs are effective to prevent youth smoking, convince smokers to quit smoking and build public awareness. Larger PHWs are significant to produce larger impact.

OA-410-28 Health warnings as integral part of health communications

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Background: There is evidence from high income countries, and growing evidence from low –and middle-income countries, of the efficacy of pictorial warnings to build risk perceptions of the health effects of tobacco, with users and the general public. As well as being a highly cost-effective policy initiative in resource constrained settings, indications are that pictorial warnings, which depict graphic imagery of diseased body parts or evoke disgust, may be the most effective in supporting behavioural changes. Hard-hitting mass media campaigns, using messages synergized with pack warning implementation, may provide optimal behavioural outcomes. Qualitative and quantitative findings from Bangladesh are explored to identify the potential added impact of synergised communication to support pictorial warnings.

Methods: Four TV announcements were developed using patient testimonials exhibiting similar conditions to those depicted on pictorial warning depictions: lung, oral and throat cancers; and childhood asthma. The announcements were pre-tested with tobacco user focus

groups in urban and rural locations of Bangladesh using a standardised set of indicators. Following pictorial warnings implementation, a national four week mass media campaign was conducted to support the policy initiative followed by an outcome evaluation. Multivariate logistic regression analyses was conducted with ‘campaign aware’ and ‘campaign unaware’ groups to identify how campaign messages rated against indicators of acceptance, perceived personalised effectiveness, discomfort, likelihood of discussing the warnings, and tobacco cessation related behaviours.

Results: Qualitative findings identified that all four testimonials rated highly against best practice indicators with both urban and rural audiences. The most graphic oral cancer testimonial scored the highest overall rating, against the 13 indicators of effectiveness. Campaign outcome evaluation findings showed significant differences in behavioural indicators by campaign aware and unaware groups with findings showing higher agreement with sentiments related to personal risk perceptions of tobacco related diseases, improved self-efficacy perceptions, and cessation related behaviours.

Conclusions: Pictorial warnings are an important policy initiative which should be stepped up in LMIC settings. Indications are that hard hitting communication campaigns which support pictorial warnings implementation can provide synergies to increase traction of this important policy initiative as well as increase dialogue, and promote cessation attempts.

OA-411-28 Are ‘loose’ cigarettes associated with increased intensity of smoking? A secondary analysis from the Global Adult Tobacco Survey, 2009-2010, India

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Background: Euromonitor International Tobacco report estimated that nearly 70% of all cigarettes are sold as single cigarettes in India, which indicates an increasing and alarming trend of single cigarette sales. World Health Organization’s (WHO) Framework Convention on Tobacco Control (FCTC) recommends countries to eliminate sale of loose cigarettes, many countries including India have not adopted this as a policy. These loose cigarettes have many important public health implications. The present study was conducted to assess whether there is an association between behavior of buying loose cigarettes and intensity of smoking.

Methods: A secondary analysis of Global Adult Tobacco Survey, India 2009-2010 data was done, on adult population age 15 years and above. The key outcome variable was ‘intensity of smoking’ defined as average

number of cigarettes smoked per day whereas the key exposure variable was 'behaviour of purchasing loose cigarettes'. Those who responded saying that they bought 1-9 cigarettes were classified as having bought loose cigarettes.

Results: Nearly 57% of current cigarette smokers (approximately 3.46 million) bought loose cigarettes. Applying this to the estimated 6.1 million smokers in India, it translates to 3.46 million. Nearly six in ten smokers purchased single cigarettes in their last purchase. The prevalence of buying loose cigarettes decreased with increasing level of education and wealth index as well as least among government employees. The intensity of smoking was 70% less among loose cigarette buyers than non buyers (OR 0.29, 95%CI 0.24-0.34). It was found to be significantly lower in rural areas (OR 0.81, 95%CI 0.68-0.97) and among females (OR 0.44, 95%CI 0.29-0.67).

Conclusion: This study showed that loose cigarette buying is associated with decreased in smoking intensity. This may be due to increased taxes leading to increased buying of single cigarettes. These findings therefore highlight a need for a comprehensive policy and further studies on loose cigarette selling. More studies are required before a concrete public health recommendation is possible.

OA-412-28 Pictorial health warnings on cigarette packs are highly effective in thinking about quitting: a case study in Punjab, India

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Background: Health warnings on cigarette packs have been established to inform smokers about the health hazards of smoking, prevent nonsmokers from initiating to smoke and encourage smokers to quit. According to the U.S. Surgeon General report, health warnings on cigarette packages are a direct, cost-effective means of communicating information on health risks of smoking to the consumers. Many countries globally have introduced pictorial warnings and many other countries are in the process of drafting regulations for pictorial warnings. The objective of present study was to estimate the impact of pack warning on cigarettes on the behavior of current smokers.

Methods: The present cross sectional study was conducted in the period of December 2015 until March 2016 in Punjab using the GATS methodology adopted during last round in 2009-2010. A three stage sampling technique was used for collecting data from three randomly selected districts (administrative divisions) of Punjab, India. A sample size of 510 individuals, 15 years and above, was divided equally into urban and rural area

with proportionate sampling on basis of subsets of age groups and gender. The questionnaire based on Tobacco Questions for Survey (TQS), a subset of key questions from GATS were used during interview with respondents.

Results: Among the current male smokers, 97.4 percent noticed the pictorial health warning on the cigarette packages, among whom 61.5 percent thought about quitting after seeing the warning label. The effect of pictorial health warning was universal (100%) in 18-24 years age-group, meaning thereby, everybody in age group of 18-24 years who watched the health warning on cigarette packs have thought of quitting. The impact of warning was almost equal in urban and rural area and also across different educational status, which demystifies the fact that literacy level and locality have significant effect on the thought process.

Conclusion: The study concludes that health warnings on cigarette packs are highly effective in thinking about quitting. Further, the effect is more pronounced in the youth, who may have just initiated smoking habit. Government of India should consider increasing the size of pictorial health warning substantially in the overall interest of public health.

16. Adult lung health: chronic obstructive pulmonary disease, chronic disease, asthma and oxygen

OA-413-28 Prevalence and risk factors of chronic obstructive pulmonary disease in a sample of adult smokers, Baghdad, Iraq, 2014

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Background: WHO estimated that chronic obstructive pulmonary disease (COPD) was the fifth leading cause of death worldwide in 2001 and will be the third by 2020. Still, COPD is an under-diagnosed cause of morbidity and mortality worldwide. In Iraq, no studies had tackled the prevalence of this problem.

Objectives: To estimate the prevalence and identify determinants of COPD among adult smokers.

Methods: This cross-sectional study was done on a convenient sample of smokers aged ≥ 40 years attending three Primary Health Care Centers in Baghdad. The subjects were directly interviewed by the researcher using a questionnaire to capture information on demographic characteristics and detailed smoking history. Lung function questionnaire (LFQ) to assess symptoms as sputum production, dyspnea and wheezing was used. Every individual score 18 or less by LFQ had a spirometry examination. If FEV1/FVC ratio is $< 70\%$, airway obstruction was considered. This was followed by a post bronchodilator spirometry to differentiate asthma from COPD. If FEV1/FVC ratio is $< 70\%$ and the amount of improvement is < 200 ml, COPD was considered. COPD severity was classified according to the Global Initiative for COPD (GOLD classification) as

Mild if FEV1 \geq 80% predicted; Moderate if FEV1 60%-80% predicted and Severe if FEV1 30 %-60 % predicted.

Results: The study sample was 325; 84% males and mean age of 51.1(\pm 10.8) years. The prevalence of COPD was 14.8% (n = 48). Mild COPD was found in 10.4%, moderate in 62.5% and severe in 27.1%. Only 12.6% (n = 8) had physician diagnosis of chronic bronchitis or COPD. Logistic regression analysis revealed two significant determinants: increasing age (P = 0.027; 95%CI 1.09-4.57) and pack year smoking (P = 0.006, 95%CI 1.59-15.97).

Conclusions: Middle-aged or older patients with positive smoking history have an increased likelihood of having underlying COPD. These patients should be counseled on the importance of smoking cessation and offered spirometry testing for COPD diagnosis.

OA-414-28 Increasing trends of COPD in persons living with diabetes: a population-based matched cohort study, 1984-2013

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Background: Chronic obstructive pulmonary disease (COPD) is a major cause of morbidity and mortality. Concurrent COPD and diabetes poses special challenge on chronic disease management. COPD and diabetes may share genetic factors. Sequential order of COPD and diabetes and factors contributing to such order may shed light on the etiology of co-existing COPD and diabetes. Information on the burden of COPD and diabetes is essential for evidence-based health care planning and service delivery.

Objectives: a) Describe the prevalence and trend changes of respiratory diseases (RD) in persons living with and without diabetes in a western province of Canada; (b) Explore the sequential orders of COPD and diabetes and factors associated with such orders.

Methods: Using Canadian Chronic Disease Surveillance System (CCDSS) data (1984-2013) and validated case definitions for diabetes and RD (asthma and COPD), we identified 182,141 persons diagnosed with diabetes and 677 953 persons without diabetes but matched (up to 1:5 ratio) to diabetes by sex, age, and residential areas. Descriptive statistics was used to evaluate the prevalence and temporal trends of RD in diabetes and non-diabetes populations. Logistic regression was used to explore the associations of diabetes and RD and factors associated with sequential orders of COPD and diabetes.

Results: The RD prevalence rates were increasing in both populations. Over the 30-year period, COPD prevalence in diabetes was higher than that in the non-diabetes (odds ratios: asthma 1.46 [95%CI 1.43 - 1.48], COPD 1.36 [95%CI 1.34 - 1.37]) after adjusting for gender, age and geographical regions. Males are more likely to have COPD (OR=1.33, 95CI 1.32 - 1.34), but less likely to have asthma (OR=0.76, 95%CI 0.75-0.77). People living in rural areas are less likely to have asthma (OR=0.65-

0.93), but northern rural residents are more likely to have COPD (OR=1.19, 95%CI 1.17-1.22). Sequential orders of COPD and diabetes are analyzed by geographical regions and demographic factors.

Conclusion: The higher prevalence and increasing trends of COPD in diabetes population pose a challenge at all levels of the healthcare system. Further analysis of healthcare utilization patterns and primary care service delivery are required for effective primary prevention and disease management.

OA-415-28 Cost of hospitalization for chronic respiratory diseases in India: how much are the poor spending?

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Background: Chronic Respiratory Diseases (CRDs) together account for an estimated burden of about 100 million individuals in India. Households spend a substantial share of their income on health care hospitalization leading to catastrophic expenditure and impoverishment. However there is little information on the impact of healthcare expenditure on households due to CRDs.

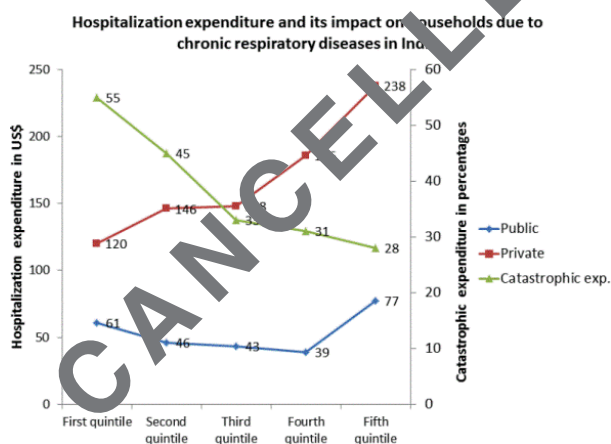
Methods: The present study analysed nationwide representative data collected by the National Sample Survey Organization (NSSO) on 'Health' and 'Education' in 2014. It reported health service utilization and health care related out-of-pocket (OOP) expenditure by income quintiles and by level of care (public or private) in the last one year. OOP expenditure exceeding 10% of annual household consumption expenditure was termed as catastrophic. Weighted analysis was carried out.

Results: A total of 1293 hospitalizations due to CRDs were recorded. Overall the cost of hospitalization for one episode of illness due to CRD was US\$ 101, with US\$ 79 and US\$ 19 among the poorest and the richest quintile respectively. There is significantly higher prevalence of catastrophic expenditure (55%) among the poorest quintile. Median private sector OOP hospitalization expenditure is nearly 3.5 times higher than the public sector. Overall, less than half (47%) of the patients with any CRD reported hospitalization in a public health facility. Nearly one-fifth of the hospitalizations are sourced from borrowings/sale of assets, which is significantly higher among the poorest quintile (22%) as compared to the richest (10%). Medicines account for 36% and 29% of public and private sector OOP hospitalization expenditure respectively. The odds of catastrophic expenditure resulting from hospitalization due to CRDs were 2.0 times higher as compared to hospital stay due to a communicable condition.

Conclusion: Strengthening of public sector health facilities is required at community level to improve access to care and reduce OOP from hospitalization due to CRDs. Promotion of generic medicines and better availability of

essential drugs will reduce OOP expenditure in public sector facilities. Regulation of private sector and publicly funded insurance coverage for preventive and curative care for the poor is the need of the hour.

Figure Hospitalization expenditure



OA-416-28 Feasibility and effectiveness of PAL proposed by the WHO for medical care for adult patients with respiratory diseases, Orizaba, Veracruz, Mexico

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Background: Despite magnitude, transcendence and impact of the respiratory diseases (RD) in Mexico, we don't have an integral focus for its prevention and control in adult patients. The Practical Respiratory Health Approach (PAL) by WHO aims to improve the diagnosis and management of RD.

Objective: To evaluate the feasibility and effectiveness of PAL through an integral health care model to patients with RD.

Methods: Site: 4 health centers (HC) in Orizaba, Veracruz, Mexico. During 08-04/2013 (Phase 1) we invited to adults >15 years old who attended the clinics. We investigated sociodemographic and clinical characteristics and obtained information from patients with medical diagnosis of RD about prescribed drugs, type of RD according to 10th DIC, co-morbidity and health practices. RD patients were visited at their home one month after to investigate clinical evolution, medical reference, information on drug provider and hospitalization. During 09/2014 we trained the HC participant

physicians on PAL model and the Guides 'AIRE'. From 09/2014 to 03/2015 (Phase 2), we repeated the procedures of Phase 1. Analysis. We described patients' characteristics by study phase by bivariate and multivariate analyses. We analyzed variables associated to clinical improvement by logistic regression analyses.

Results: During Phase 1, we recruited 3238 participants, 365 (11.27%) with RD; during Phase 2, 2755 individuals, 373 (13.54%) with RD. The more frequent diagnoses were: acute tonsillitis 197 (30.45); influenza-like disease 36 (5.56%); otitis media; upper respiratory tract infection and emphysema 16 (2.47%). During phase 2 we observed greater frequency of clinical improvement (65.6% vs. 55.6%), reduction of prescription of steroids (1.13% vs. 1.61%), broad spectrum antibiotics (0.00% vs. 1.32%) and bronchodilators (3.34% vs. 6.4%). The patients had improved access to the drugs at pharmacies of HC (74.20% vs. 95.48%). Compared to the standard of care, the RD patients on the proposed model, were more likely to have clinically improvement one month later (OR 2.4; CI 95% 1.18, 4.89; $P = 0.016$).

Conclusions: It is feasible to implement the PAL model, and the data suggest its effectiveness by improved treatment results and drug access.

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OA-417-28 The development of a lung health awareness-raising programme in Masindi province, Uganda

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Background and challenges to implementation: Chronic lung disease is common but under-reported in sub-Saharan Africa. Following a survey in rural Uganda which found 16% of the adult population had COPD, we developed a lung health awareness programme to detect and prevent chronic lung disease. This is a two-year train-the-trainer programme conducted by health care workers (HCWs) led by the district health officer in Masindi district.

Intervention or response: Working with HCWs who had conducted the Fresh Air Uganda survey, we implemented a train-the-trainer programme for HCWs who taught village health teams (VHTs) to teach their communities. We held a series of meetings to develop the project strategy and contents of the education materials. Preliminary education materials were shown to senior clinicians, administrators (including the Minister for Health and DHO in Masindi) through all grades of clinicians to VHTs and villagers. Incorporating all feedback in an updated programme, the first group then taught other HCWs and again adapted the materials. Final educational materials covered: What is lung health?, How the lung gets damaged?, Lung growth and development and Preventing harm by reducing

exposure to tobacco smoke and biomass smoke. We designed radio messages for broadcast on talkshows and radiospot adverts locally. Evaluation methods included designing knowledge questionnaires for use before and after training for HCWs and the population.

Results and lessons learnt: Educational materials for use in training HCWs and VHTs using desk-aid flip-over charts, and posters have been designed and approved by the Ministry of Health. The target was to train 10 HCWs in the first group and 12 completed this. These 12 then trained 47 HCWs, and VHT training is ongoing with over 100 so far completing. We have developed and administered knowledge questionnaires.

Conclusions and key recommendations: Using a ground upward approach we involved the local health care systems and HCWs to develop and deploy a train-the-trainer programme which is continuing. The educational materials were designed by the team are now approved for national use. The materials are available for wider use including in our international projects, in pulmonary rehabilitation and in midwifery training.

OA-418-28 Assessment of asthma control and risk factors for poor asthma control among patients seen at a referral hospital, Addis Ababa, Ethiopia

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Background: Uncontrolled asthma negatively impacts patients, families and the community, and identifying risk factors can greatly modify these adverse effects. The level of asthma control and risk factors for poor asthma control are unknown in Ethiopia and the focus of this study.

Methods: In this cross-sectional study, 182 consecutive subjects with a physician diagnosis of asthma seen in chest clinic at Tikur Anbesa Specialized Hospital (TASH) between July and December, 2015 were included. Subjects were enrolled if they fulfilled inclusion criteria. Demographics, respiratory symptoms, medication, and potential risk factors for poor control were obtained from the clinic records. Lung function was measured using a Diagnostic EasyOne Plus model 2001 SN spirometer. Asthma control was assessed based on GINA asthma control guidelines. The study protocol was approved by the institutional review board and all subjects signed informed consent. SPSS 20 was used to analyze the data.

Results: Of the 182 subjects, 68.1 % were female; the mean age was 52±12 years and the median duration of asthma was 20±12.7 years. One hundred and five subjects (57.7%) had daytime symptoms (wheeze or dyspnea) more than twice per week, 117 (64.3%) had nighttime awakening due to asthma, and 52 (28.6%) had activity limitations due to asthma. One hundred and five

subjects (57.7%) used inhaled corticosteroids (ICS), 19(10.4%) used a combination ICS and a long acting beta agonist, and 173 (95.1%) used inhaled salbutamol. Oral steroids were used by 25 (13.7%) of the group. Of those with pulmonary function testing (92), FEV1 was < 60% in 41 (44.6%), 60-80% in 27 (29.4%), and >80% in 24 (26%). Only 44 (24.2%) subjects had well-controlled asthma; 41 (22.5%) were partially controlled and 97 (53.3%) were uncontrolled. Use of biomass fuel for cooking (OR 1.99, 1.06-3.72), longer duration of asthma (≥ 21 year) (OR 3, 1.08-8.33), incorrect inhalation technique (OR 3.05, 1.58-5.90) and asthma exacerbation in the last 12 months (OR 2.50, 1.40-4.60) were found to be associated with uncontrolled asthma.

Conclusions: Most asthmatics attending chest clinic at TASH had poorly controlled asthma. Several risk factors for poor asthma control were identified. Improved asthma control is possible through directed interventions.

OA-419-28 Oxygen therapy in a resource-limited setting: a time-series analysis of oxygen requirement and use in acutely unwell adults in Malawi

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Background: Oxygen (O₂) is an 'essential medicine', yet demand frequently outstrips supply in hospitals in resource-limited settings. 10% of acutely ill adults in the Emergency Department (ED) in Malawi are hypoxic (pulse oximetry [SpO₂]) < 90%). O₂ is delivered via concentrators, but availability is limited by insufficient concentrator numbers and difficulties with maintenance of machines. The duration of O₂ requirement in such settings is unknown. We observed hypoxic adults admitted from the ED to determine their time on therapy, and their outcome.

Methods: Hypoxic participants identified in the ED were monitored at least twice daily by SpO₂ and vital signs until one of three clinical endpoints was reached: stability - 2 consecutive readings of SpO₂ ≥ 90% on air; discontinuation of O₂ prior to stability; death while using O₂.

Results: 56 patients were enrolled, 23 (41%) were female. 48 patients (86%) survived the observation period. Ten patients (18%) had O₂ discontinued before O₂ stability was achieved. Median duration of O₂ use in stable patients was 20.6 hours (IQR 10-50). Eight (14%) patients died during the study period, after a median 11 hours (6-19). Survivors tended to have SpO₂ which

normalised on therapy ($n = 50$ [89%]) compared with those who died ($n = 6$ [75%]).

Conclusions: Deaths occurred early in patients whose hypoxia persisted despite initial O₂ therapy. High demand for O₂ concentrators was the likely reason for discontinuation of O₂ in hypoxic patients. In a resource-limited setting, these time-series data on oxygen requirement can usefully inform the provision and allocation of this essential drug.

Table Duration of oxygen use & clinical endpoints

	Overall ($n = 56$) n (%)	O ₂ 'stability' achieved ($n = 38$) n (%)	O ₂ discontinued prior to 'stability', survived ($n = 10$) n (%)	Died ($n = 8$) n (%)
Initial SpO ₂ on Air, % (SD)	77 (13.6)	78.7 (11.7)	77.3 (14.2)	68.9 (19.6)
Respiratory rate, mean (breaths per minute) (SD)	23.8 (5.6)	22.9 (4.3)	24.4 (8.1)	27.3 (6.9)
Duration actively observed, median hours (IQR)	30.3 (19.0-58.3)	33.4 (21.3-71.5)	41.4 (16.1-70.9)	10.7 (6.0-18.5)
Time to stable normoxia, median hours (IQR)	-	20.6 (10.4-50.3)	not achieved	not achieved

OA-420-28 Diagnostic performance of chest computed tomography for the localization of bleeding site in patients with hemoptysis

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Background: This study was to evaluate diagnostic performance of chest CT and to suggest for the localization strategy of the bleeding site in patients with hemoptysis.

Methods: Between January 2005 and July 2009, the chest CT findings were retrospectively reviewed 161 patients with hemoptysis. The lobe having the most prominent ground glass attenuation (GGA) or specific lesions that can cause pulmonary hemorrhage on chest CT were defined as the bleeding site. Fiberoptic bronchoscopy (FOB) findings were defined as the standard reference for bleeding site.

Results: The diagnostic accuracy (DA) and concordance rate of the most prominent GGA was higher than those of the specific lesions on chest CT for the localization of the bleeding site (DA = 79.5% vs. 60.9%, $K = 0.751$ vs. 0.448). Among the specific lesions, lung cancer and

fungal ball showed relatively high concordance rates to FOB (100% = 3/3 and 89% = 8/9). The localization of the bleeding site between FOB and chest CT revealed almost perfect agreement ($K = 0.904$).

Conclusions: The localization of bleeding site in patients with hemoptysis could be determined by the chest CT findings such as the most prominent GGA and specific lesions including malignancy and fungal ball.

17. HIV-TB Late-Breaker Session

OA-2981 Effectiveness of combination intervention package on initiation of antiretroviral therapy among patients with tuberculosis and HIV (TB-HIV)

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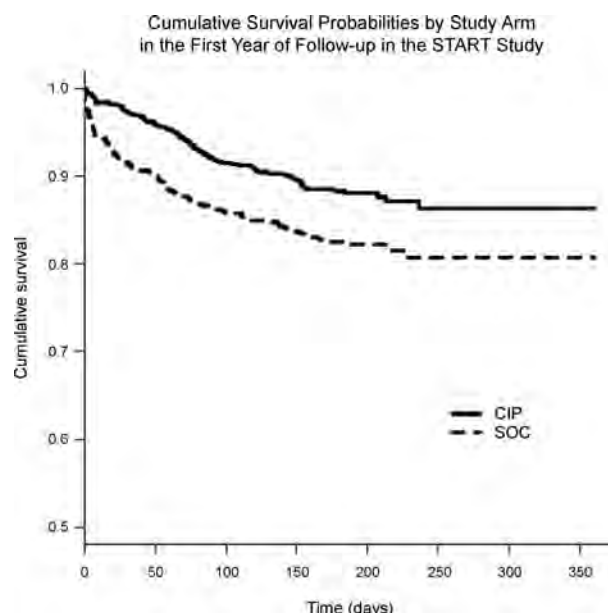
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Background: Early antiretroviral therapy (ART) initiation during TB treatment improves survival; however, implementation is suboptimal. The START Study aimed to evaluate the effectiveness of a combination intervention package (CIP) to improve ART initiation and TB treatment success among TB-HIV patients in Lesotho.

Methods: Twelve clinics were site-randomized to receive CIP or standard of care (SOC). CIP included: 1) nurse training and mentorship using a clinical algorithm; 2) transport reimbursement; 3) health education by village health workers (VHW) for patients and treatment supporters; and 4) adherence support using text messaging and VHW. Routine data were abstracted for all TB-HIV patients at the clinics. Generalized linear mixed models were applied to test for differences between study arms for ART initiation and TB treatment success; frailty models were used to examine differences in survival.

Results: Among 1233 TB-HIV patients enrolled between 04/2013 and 03/2015, mean age was 38.6 ± 10.9 y; median (IQR) CD4 count among 246 ART initiators with available data was 157 (67-323). 86% had pulmonary TB; 84% were new TB cases; and 30% were on ART at TB treatment initiation. Among 865 patients who were not on ART at TB treatment initiation, 96% (486/504) of CIP patients initiated ART during TB treatment vs. 86% (311/361) of SOC patients (RR 1.12, 95% CI 0.97-1.30). Median (IQR) time to ART initiation was 15 (14-23) days in CIP and 25 (15-37) days in SOC. TB treatment success was achieved by 81% (577/713) in CIP vs. 73% (379/520) in SOC (RR 1.11, 95% CI 0.98-1.26); overall 15% of patients died. CIP patients had a lower hazard of death than SOC patients (HR 0.64, 95% CI 0.47-0.86) (Figure).

Conclusions: The combination intervention package significantly improved survival of TB-HIV patients. Timely HIV diagnosis and ART initiation are essential to mitigate the high mortality associated with HIV-related TB.



OA-3012 Accessibility of HIV-TB services is a facilitator for TB screening amongst PLHIV: a case study from Central India

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Background: The National Policy in India recommends intensified TB case finding amongst PLHIVs, including prioritized offer of Xpert MTB/RIF services to all PLHIV presumptive-TB cases for early diagnosis. During April 2015-March 2016, total 8011 PLHIV were referred from ART-centres to RNTCP in Madhya Pradesh (MP), of which 5% were diagnosed as TB (HIV-TB Line-listing). A possibility of PLHIV presumptive-TB cases not reaching Designated Microscopy Centres (DMC) for TB-diagnosis was explored in one district of MP.

Method: A case-study was undertaken to understand the facilitators and hindrances for TB screening amongst PLHIV presumptive-TB cases in Sagar district, MP using record reviews and in-depth discussions with healthcare providers and PLHIVs. Narrative analysis was used to document key elements of TB diagnostic and management process amongst PLHIVs referred from ART-centre.

Results: During 2015, total of 455 PLHIV presumptive-TB cases were referred from ART-centre, located at Bundelkhand Medical College, Sagar to the District TB Centre (DTC), which also provides Xpert services for DR-TB-diagnosis. Of these, only 65% were tested using Xpert, revealing quite a large proportion of cases being missed. During discussions, both providers and PLHIVs felt that often patients referred for TB-screening get lost or are missed due to accessibility issues; thus posing a potential risk to community by spreading the Mycobac-

teria. Inconvenience in accessing services was perceived by majority PLHIVs referred for TB-diagnosis, since they had to walk 2km to reach DTC. A DMC within Medical College premises was initiated in December-2015, thereby an improved accessibility for TB-symptomatics referred from ART-centre. An analysis of HIV-TB data reveals that with an improved access for TB diagnostic services, there has been a considerable decrease in proportion of PLHIV presumptive-TB cases being missed from 35% in 2015 to 6% during January-May 2016.

Conclusions: Findings emphasise a need for better access and patient-friendly services including improved counselling for increased demand for HIV-TB services. There is also a need for strengthening supervision and linkages between HIV and TB services/programmes.

Table ART and RNTCP cross-referral, Sagar District

	ART to RNTCP referral n	Tested with Xpert n (%)	MTB detected n (%)	Cases missed n (%)
Jan-Dec 2015	455	297 (65%)	19 (6%)	158 (35%)
Jan-May 2016	109	103 (94%)	8 (8%)	6 (6%)

OA – 3048 Potential impact of antiretroviral therapy on tuberculosis incidence among people with and without HIV in 26 countries, sub-Saharan Africa, 2010–2014

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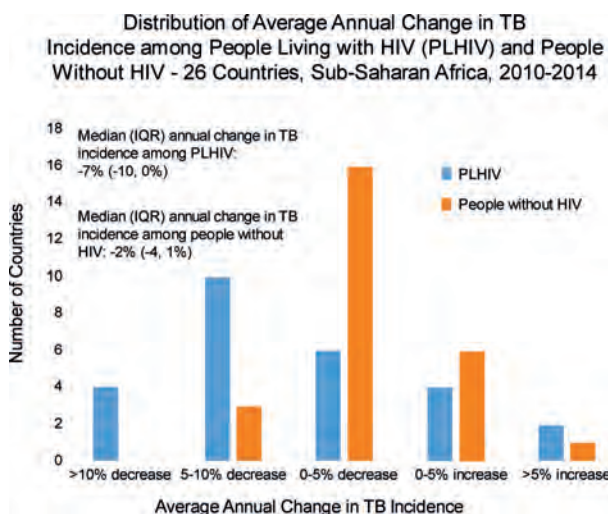
Background: Human immunodeficiency virus (HIV) is a major driver of the tuberculosis (TB) epidemic in sub-Saharan Africa. Although antiretroviral therapy (ART) has been shown to protect against TB at the individual level, its impact on TB incidence in this region has not been well-studied. We conducted an ecological analysis to describe the relationship between ART coverage and reported TB incidence, by HIV status, in countries of the World Health Organization (WHO) Africa region.

Method: We combined TB notification data from WHO, HIV prevalence estimates from the Joint United Nations Programme on HIV/AIDS (UNAIDS), and population estimates from the United Nations Population Division to estimate reported TB incidence among people living with HIV (PLHIV) and people without HIV, by year, during 2010-2014. Coverage of ART for each country during this period was obtained from UNAIDS. Countries were included in analysis if, during 2010-2014, they had both ≥ 3 years of HIV prevalence estimates and TB notification data in which $\geq 75\%$ of TB cases had an HIV test result.

Results: Of 47 countries in the WHO Africa region, 26 (55%) met inclusion criteria. All of these countries increased ART coverage during 2010-2014 with 12 (46%) countries increasing ART coverage by $\geq 20\%$. Fifteen (58%) countries had an average ART coverage during this period of $\geq 30\%$. Overall, from 2010 to

2014, PLHIV demonstrated greater average annual decreases in TB incidence compared to people without HIV (Figure). Average annual decreases in TB incidence >10% occurred only in PLHIV. The median annual change in TB incidence among PLHIV was -7% (interquartile range [IQR] -10 to 0%), whereas the median annual change in people without HIV was -2% (IQR -4 to 1%).

Conclusions: ART uptake has been increasing and TB incidence decreasing, especially among PLHIV. These trends suggest that ART scale-up may have reduced TB incidence among PLHIV in this region.



OA- 3106 Do high expression MIF alleles confer protection against active tuberculosis?

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Background: Host immunity is crucial for control of TB. Macrophage migration inhibitory factor (MIF) is an innate cytokine that is encoded in a functionally polymorphic locus; allelic variants show population stratification and association with TB progression. Here we present the prevalence of MIF risk alleles and their association with TB in HIV-positive South African patients.

Method: In two cohorts comprised of HIV-positive patients with active laboratory-confirmed pulmonary TB and controls without active disease recruited in Durban and Tugela Ferry, South Africa, we collected demographics, clinical information, serum and blood

samples to determine MIF cytokine levels and two MIF promoter polymorphisms: a functional -794 CATT5-8 microsatellite (rs5844572) and a closely associated -173 G/C SNP (rs755622).

Results: In the Durban cohort, among 196 HIV-positive patients with a median age of 34 (IQR 29-40) and a median CD4 count of 142 (IQR 80-260), 69.7% were female and 120 (45.5%) had active pulmonary TB. In the Tugela Ferry cohort, 165 HIV-positive patients were enrolled with a median age of 36.5 (IQR 29 - 46) and a median CD4 count of 91 (IQR 38.5-308); 79 (50%) were female and 100 (60.6%) had active pulmonary TB. Polymorphism assessment at the MIF promoter demonstrated higher prevalence of the low expression haplotype (-794 CATT5/-173 G) among 196 TB cases than 94 controls without active TB ($P=0.04$; OR=1.38). Among all HIV-positive patients regardless of TB status, circulating MIF levels negatively correlated with CD4 count ($P=0.016$).

Conclusions: A low expresser MIF haplotype occurs more commonly among TB cases than controls. As South Africans show the highest global prevalence of low expression MIF alleles, this finding suggests a contribution of functional MIF polymorphisms to the high prevalence of TB in this population. We further report a novel inverse relationship between serum MIF levels and CD4 count, suggesting a potential relationship between MIF and HIV level of immune suppression. Assessment of MIF genotype may help TB risk stratification and circulating MIF protein levels may offer prognostic information in HIV-positive patients. Pharmacologic augmentation of MIF effector pathway, currently in pre-clinical development, may be a useful therapeutic strategy in low genotypic MIF expressers.

OA-3110 Immunological recovery in TB-HIV co-infected patients on antiretroviral therapy: insight into strategy for tuberculosis preventive therapy

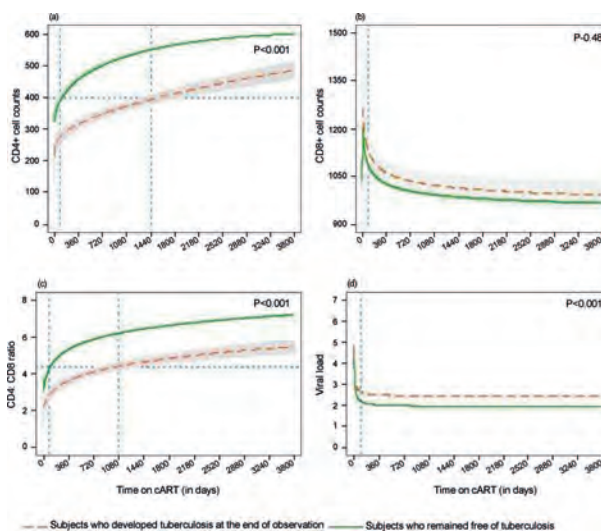
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Background: We aimed to investigate the long-term immunological and virological dynamic in cART-treated HIV-infected patients in relation to development of active TB.

Methods: Data was extracted from a multicenter cohort for the HIV clinical surveillance in Germany. We analyzed the trajectories of CD4+, CD8+ cell counts, CD4:CD8 ratio and viral load over 10 years in patients who remained free of TB vs. those who developed TB. To detect the best-fit model, we applied multivariable fractional polynomials in generalized estimating equations.

Results: A total of 10 772 HIV-infected patients including 1.3% ($n=144$) patients who developed TB were eligible for our analysis. The majority of TB-HIV cases (65%) occurred within the first 3 years of cART. In a model adjusted for sex, geographical origin, HIV-transmission routes, age and year of cART initiation, progression to active TB was a significant predictor for the trajectories of CD4⁺ cell counts [RC (regression coefficient) -72.2 ; CI (95% confidence interval) -108.4 to -36.0], CD4:CD8 ratio [RC -0.1 ; CI -0.2 to -0.1] and viral load [RC 0.3 ; CI 0.2 to 0.5], but not for CD8⁺ cell counts [RC 35.9 ; CI -63.0 to 134.9]. Patients who remained free of TB had showed an excellent immune recovery and reach high CD4:CD8 ratio (>0.44) and CD4⁺ cell counts (>400 cell/ μ l) rapidly in the initial 3 months of cART, while patients who developed TB had required considerable time (3 and 4 years respectively) to reach this immune level.

Conclusion: Our findings emphasize the importance of CD4:CD8 ratio and CD4⁺ cell counts dynamics under cART as a valuable marker for development of HIV-associated TB. HIV-infected patients who developed TB had showed poor immune response to cART and adjunctive TB preventive therapy is likely to be of particular benefit for those patients with immunological thresholds less than 0.44 CD4:CD8 ratio and 400 CD4⁺ cell/ μ l.

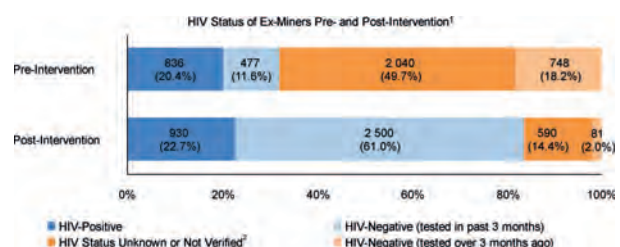


testing (HCT) and passive TB case finding are the primary modes for identifying disease among this population, resulting in delayed or missed diagnosis. Scalable, community-based strategies to reach ex-miners and their families with HIV and TB diagnostic services are needed.

Methods: A 5-month TB and HIV campaign targeting ex-miners and their family members was conducted in 4 districts of Lesotho in early 2016, the largest HIV-TB screening effort targeting this population at the community level in-country to date. Mobilization was carried out by a community-based organization that works with miners and ex-miners. The service package included HCT, TB symptom screening, sputum collection and transport for testing on the Xpert MTB/RIF platform, isoniazid preventive therapy initiation, follow-up for HIV and TB treatment initiation and household contact investigation.

Results: Activities reached a total of 5786 people, of whom 5036 (87.0%) were ex- or active miners and 750 (13.0%) were family members. Of 4101 ex-miners who disclosed their HIV status, 1313 (32.0%) were known HIV-positive or had tested HIV-negative in the previous 3 months, and thus not recommended for HCT according to national guidelines. Of the remaining 2788, 2117 (75.9%) agreed to HCT (see Figure). Of 4432 ex-miners screened for TB symptoms, 84 (1.9%) were already on TB treatment, and 139 (3.1%) ex-miners had TB symptoms and submitted sputum samples for testing.

Conclusion: Collaborative outreach with a community-based organization expanded the number of people reached with HIV and TB diagnostic services, resulting in a significant increase in the proportion of individuals with known HIV status. The rate of people already on TB treatment was higher than in past efforts. Given the population, lack of access to chest X-ray likely limited TB screening yields.



¹ This includes 4,101 (82.0%) of the 5,004 registered ex-miners who were willing to disclose their HIV status.
² Not Verified means the individual did not have their bukana (health passport) on hand to officially confirm past testing results. This made up 35% of the 2,040 individuals in this sub-group pre-intervention.

OA-3112 Community-based TB screening and HIV testing for ex-miners in Lesotho

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Background: Ex-miners are a high risk group for HIV and TB in Lesotho, yet voluntary HIV counselling and

18. The tide is high: TB and comorbidities

OA-421-28 Tuberculosis and diabetes: trends in hospitalizations and impact on health care costs in the USA

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Background: Among the 22 high-burden tuberculosis (TB) countries, an estimated 7.5% of the TB burden has been attributed to diabetes. Given the burgeoning global diabetes epidemic, a national sample was used to determine secular trends in the proportion of hospitalized TB patients with co-morbid diabetes and to explore the impact of diabetes on mortality and healthcare utilization among patients hospitalized with TB in the US.

Methods: The Healthcare Cost and Utilization Project's National Inpatient Sample (NIS) database was used to construct a cohort of all hospitalizations with a primary diagnosis of TB (International Classification of Diseases, 9th Revision, Clinical Modification [ICD-9-CM] codes 010.xx - 018.xx) and the subset with diabetes (ICD-9-CM codes 250.x0 - 250.x3) during the years 2000 through 2011. Each year, the NIS collects information from about 1000 US hospitals. Secular trends were assessed using the Cochran-Armitage test for trend. Inpatient all-cause mortality, hospital length of stay (LOS) and total inpatient charges were compared among primary TB hospitalizations with and without diabetes using the χ^2 test or *t*-test. Logistic and linear regression models were used to control for potential confounders.

Results: Of 102 072 primary TB hospitalizations identified, 16 796 (16.5%) also had diabetes. Over the 12-year period, the rate of primary TB hospitalizations without diabetes decreased by 50% ($P < 0.001$). The rate of with primary TB hospitalizations with diabetes increased by 27.6% ($P < 0.001$); the increase was exclusively due to an increase in type 2 diabetes which was 2- to 19-fold more prevalent among primary TB hospitalizations than type 1 diabetes, depending on the year. Diabetes was associated with a longer LOS (avg 1.5 days, $P = 0.003$) and on average an additional \$20 000 per hospitalization (\$68 468 vs. \$48 495). Annual inpatient mortality among TB hospitalizations was similar in both groups (4.11% vs. 3.8%, $P = 0.49$), and did not change over time ($P = 0.49$).

Conclusions: In this US cohort, primary TB hospitalizations with co-morbid diabetes increased significantly and were associated with longer LOS and higher inpatient costs. The expanding global diabetes epidemic may unfavorably impact hospitalizations and healthcare costs among TB patients, especially in TB-endemic countries.

OA-422-28 Risk of death and/or poor treatment outcomes among persons with tuberculosis and diabetes in high TB and diabetes burden countries: a systematic review

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Background: The impact of diabetes mellitus (DM) in persons with tuberculosis (TB) has recently received increased attention globally. A systematic review (studies published through December 2010) examined the association between DM and TB treatment outcomes, but the majority of included studies were conducted in developed countries. Given the concern over the impact of TB/DM in TB and DM high burden countries (TBhbc & DMhbc), many new studies have been published recently. We systematically reviewed the literature through 2015 to determine if the association differs by TBhbc and DMhbc.

Methods: The search was conducted in 6 main bibliographic databases and all languages. We included cohort and case-control studies investigating treatment outcomes (TBTO) between TBDM and TB non-DM patients. Two reviewers independently screened abstracts, full-texts, and extracted data. The methodological quality and risk of bias of the included studies were assessed according to Newcastle-Ottawa Scale and Cochrane review guidelines. Random-effect meta-analysis was used for data synthesis; main analyses were stratified by TBhbc and DMhbc.

Results: The literature search yielded 16770 articles; 94 full-texts were reviewed; of these 27 studies reported TBTO from TBhbc and 46 from DMhbc; 12 from TBhbc & DMhbc. TBDM patients had an increased risk of death compared with TB patients in the pooled analysis regardless the setting (Pooled Relative Risk pRR = 1.7, 95%CI 1.4-2.1; I^2 :79.9); pRR = 2.0 (95%CI 1.4-2.8) in TBhbc; pRR = 1.9 (95%CI 1.4-2.5) in DMhbc; and pRR = 2.1 (95%CI 1.5-2.9) in TBhbc & DMhbc. TBDM patients had higher risk of poor outcome (treatment failure or death) compared with TB non-DM patients (pRR = 1.8, 95%CI 1.5-2.2); pRR = 2.5 (95%CI 1.6-3.8) in TBhbc; pRR = 2.0 (95%CI 1.4-2.8) in DMhbc; and pRR = 2.5 (95%CI 1.5-4.2) in TBhbc & DMhbc. The pRR for culture positivity at 2-3 months was 1.6 (95%CI 1.2-2.1) among TBhbc; 1.6 (95%CI 1.2-2.2) in DMhbc; and 0.9 (95%CI 0.5-1.5) in TBhbc & DMhbc.

Conclusions: TBDM patients had higher risk of unsuccessful TB treatment outcomes compared with TB non-DM patients regardless of the burden of TB and DM in study countries. TB programmes should address an adequate glycemic management among TBDM patients in all countries to improve TB treatment outcomes.

OA-423-28 Chronic kidney disease progression and risk of tuberculosis: a cohort study

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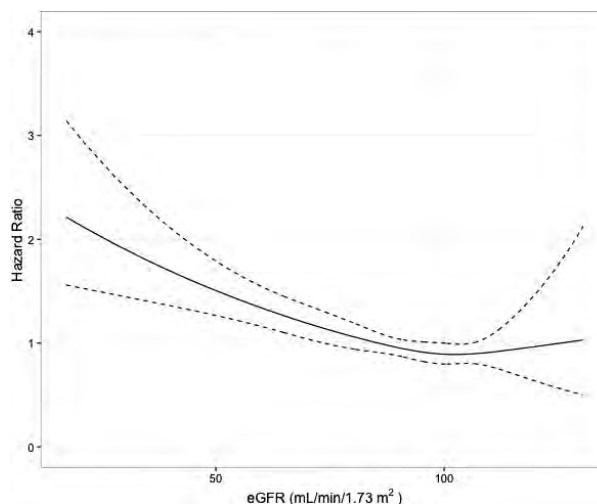
Background: Patients with end-stage renal disease (ESRD) are known to have increased risk of active tuberculosis. However, no studies have investigated the tuberculosis risk in pre-ESRD chronic kidney disease (CKD) patients, and the relationship between CKD progression and tuberculosis risk remains unclear.

Methods: We conducted a cohort study with 116 637 participants of a community-based health screening service in Taiwan from 2005-2015. We calculated estimated glomerular filtration rate (eGFR) from serum creatinine and the Chronic Kidney Disease-Epidemiology Collaboration Equation. Tuberculosis cases were identified from the national tuberculosis registry. We fitted a cox regression model to calculate the hazard ratios (HRs) for each stage of CKD, adjusting for age, sex, smoking, alcohol use, diabetes, body mass index, and socioeconomic indicators. We used spline regression to investigate the dose-response relationship between eGFR and tuberculosis risk. We calculated population attributable fractions (PAFs) of CKD using the prevalence of different CKD stages and estimated HRs.

Results: After a median follow-up of 9.2 years, 884 cases of tuberculosis occurred. Compared to non-CKD subjects, the adjusted HR was 1.30 (95% confidence interval [CI] 1.06-1.60) for stage 1 and 2 CKD patients, 1.51 (95%CI, 1.24-1.84) for stage 3, 2.09 (95%CI 1.20-3.65) for stage 4, and 3.61 (95%CI 1.61-8.09) for stage 5. In the spline regression model, tuberculosis risk increased monotonically with decreasing eGFR when eGFR was below 90 ml/min/1.73m² (Figure). The PAF of all stages of CKD was 5.61%, while the PAF of stage 5 CKD was 0.26%.

Conclusions: The results of our study show an increased risk of tuberculosis even in early stages of CKD and suggest a dose-response relationship between progression of CKD and risk of tuberculosis. These findings can guide tuberculosis screening strategies to target patients at various stages of CKD, a disease whose prevalence is on the rise globally.

Figure eGFR vs. TB hazard ratio from spline model



OA-424-28 Prevalence and clinical relevance of respiratory viruses among tuberculosis patients and household controls in Tanzania

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Background: The current evidence shows respiratory viruses can impair clearance of mycobacteria and affect the clinical presentation and outcomes. We aimed to assess the prevalence of respiratory viruses among TB patients and controls among TB patients in a high TB incidence country.

Methods: We recruited microscopy smear-positive adult (≥ 18 years) TB patients and household controls without TB from an on-going TB cohort study in Dar es Salaam (TB-DAR) enrolled between November 2013 and June 2015. We analyzed nasopharyngeal swabs (Copan) taken at the time of recruitment using a multiplex real-time PCR with a panel of 16 respiratory viruses (Seegene Anyplex RV16, South Korea). TB score as an indicator for clinical severity was based on 13 clinical symptoms and physical examination. Data were analyzed by χ^2 tests and logistic regression models.

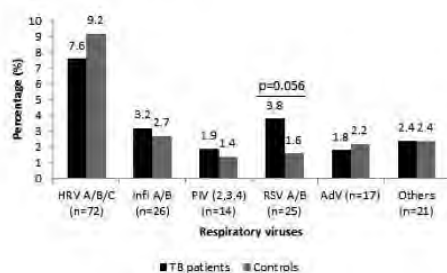
Results: We analyzed 500 TB patients and 371 household contact controls. The median age was 34 years (Interquartile range [IQR]: 27-42 years); 515 (59.1%) were men and 168 (19.7%) of 854 participants were HIV-positive. Overall prevalence of any respiratory viral pathogen was 18.6% (95% confidence interval [95%CI]: 16.1-21.3%). The most frequently detected viruses were Human Rhinovirus A/B/C (74, 8.3%), Influenza A/B (26, 3.0%) and Respiratory Syncytial Virus A/B [RSV A/B] (25, 2.9%) (Figure). Double virus detection was observed in 18 (2.1%) of the participants. There was no statistically significant difference in virus detection between TB patients and controls (94 patients

[18.8%] vs. 67 controls [18.1%]; $P = 0.7$). Among TB patients, detection of any virus tended to be associated with sputum smear acid fast bacilli (AFB) grading $\geq 2+$ (adjusted odds ratio [aOR] 3.00, 95%CI 1.18-7.68, $P = 0.057$) and with a moderate/severe TB score (≥ 6 TB score) (aOR 1.53, 95%CI 0.95-2.46, $P = 0.082$). No association was found with age, sex, HIV status, income level, occupation, educational level, smoking and number of people living in the same household.

Conclusions: Respiratory viruses were equally distributed among TB patients and household controls. TB patients with high mycobacterial load and severe TB symptoms at diagnosis were likely to have respiratory viruses. Further research is needed on effect of respiratory viruses on TB treatment outcomes.

Figure Tuberculosis and respiratory viruses

Figure: Frequency distribution of respiratory viruses among 500 TB patients and 371 controls at the time of TB diagnosis or recruitment. HRV, Human Rhinovirus; Infl, Influenza; PIV, Parainfluenza 2/3/4; RSV, Respiratory syncytial virus; Adv, Adenovirus; Others, Coronavirus OC43/NL63 & 229E; Metapneumovirus; Enterovirus.



OA-425-28 The effect of risk factor control on tuberculosis in Taiwan: a modelling study

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Background: In the new End TB Strategy, management of TB risk factors, including smoking, alcohol use, diabetes, and underweight, is considered to be a critical component. Few studies have assessed the impact of reducing multiple risk factors on future trend of TB incidence at the national level.

Methods: We used a compartmental model with age structure for TB transmission in Taiwan to evaluate the impact of risk factors. The parameters in the model were adjusted by the weighted average of the relative risk and joint distribution of these risk factors. We obtained the joint prevalence of risk factors from periodic National Health Interview Surveys and constructed possible future scenarios of risk factors based on WHO's Noncommunicable Disease (NCD) control targets. The model was calibrated to the trend of TB incidence in Taiwan. The effect of risk factors control was estimated by comparing the percentage of reduction in TB incidence under different scenarios between 2015 and 2035.

Results: If current TB control measures remain unchanged and all the risk factors follow the current trend

(decreasing prevalence of smoking, increasing prevalence of alcohol use and diabetes), cumulative reduction of TB incidence would be 4.5% by 2035. If the NCD targets of reducing alcohol use, stopping the rise of diabetes and ending hunger are reached, the cumulative reduction in TB incidence would be 13.1%, 14.2% and 7.1%, respectively. Achieving the three targets simultaneously would result in 23.2% reduction in TB incidence. On the other hand, if the prevalence of smoking stops decreasing, TB incidence would only reduce by 1.0% in 2035.

Conclusions: The results shows that controlling TB-related risk factors at the population level could reduce TB burden and help to achieve the target of the End TB strategy.

Figure Scenarios of risk factor control

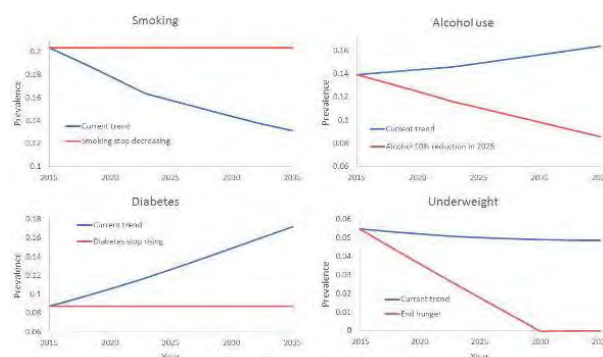


Figure 1: Scenarios of risk factor control

OA-426-28 Challenges in diagnosing diabetes among those with newly diagnosed pulmonary TB: diagnostic variability according to diabetes disease severity

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Background: TANDEM is a multicentre European Commission funded study (www.tandem-fp7.eu) designed to identify optimal ways to screen for diabetes mellitus (DM) in TB patients. This study evaluated the performance of screening tools for DM in newly-diagnosed TB patients.

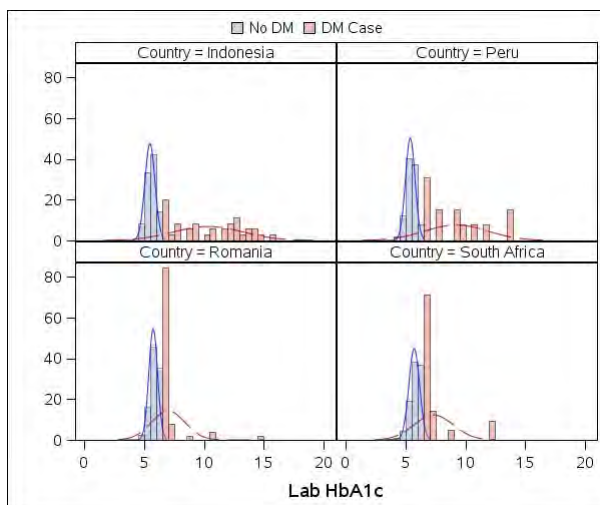
Methods: TB patients were included from Indonesia ($n = 636$), Peru ($n = 417$), Romania ($n = 394$) and South Africa ($n = 257$). New DM cases were identified using laboratory HbA1c. The diagnostic accuracy of random blood glucose (RBG), point of care (POC) HbA1c

testing, and other anthropometric measurements was assessed.

Results: 121 new DM cases were identified giving an undiagnosed DM prevalence of 7.1% (95%CI 6.0-8.4). The distribution of laboratory HbA1c for those with and without DM varied substantially by centre (Figure). POC HbA1c testing combined with age achieved the highest AUROC ($C = 0.89$, 95%CI 0.86-0.92), although POC HbA1c alone performed equally well ($C = 0.88$, 95%CI 0.85-0.91). RBG also performed well in combination with age and without ($C = 0.84$, 95%CI 0.80-0.88) and $C = 0.82$, 95%CI 0.78-0.86), respectively). POC HbA1c $>6.0\%$ identified new DM cases with 92.3% sensitivity and 75.5% specificity. RBG >6.1 mmol/l identified new DM cases with 76.0% sensitivity and 66.4% specificity. The diagnostic accuracy of POC HbA1c and RBG varied between centres. In Indonesia and Peru POC HbA1c identified new DM cases with 100% sensitivity and 62.6% specificity; in Romania and South Africa the same figures were 43.7% and 85.5%. For RBG, in Indonesia and Peru sensitivity was 89.4% and specificity 73.5%, whereas in Romania and South Africa the same figures were 58.3% and 58.5%.

Conclusions: POC HbA1c, and in some settings RBG, offer strong diagnostic accuracy for identifying new DM cases in TB patients. However, the accuracy depends on the severity of undiagnosed DM in the population and a one size fits all approach may not be appropriate.

Figure HbA1c distribution by country



OA-427-28 A rapid assessment of the nutritional status of TB patients and the integration of a nutrition assistance program in Ethiopia

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Background: Nutritional problems among TB patients are one of the key comorbid conditions that fuel the epidemic and create deleterious impact towards TB control. This national level rapid assessment aims to measure the degree of malnutrition in TB patients and assess the implementation status of integrated nutritional assessment counseling and support for TB.

Methods: The assessment was conducted from November, 2014 to January, 2015 using descriptive cross-sectional study design. 54 Health facilities were selected using random sampling procedure from the list of Health facilities providing TB services in 11 regions. Study participants were selected by proportional stratified sampling methods with sample size of 1258 TB patients on treatment. Data collection was conducted using both quantitative and qualitative methods. Quantitative data were collected on 913 TB patients by measuring BMI of patients using standard anthropometric measurement tools and interpreted using WHO reference charts while qualitative data were gathered from 54 focus group discussion with 295 patients and by conducting key information interviews with 81 TB cases using semi-structured questions.

Results: 57% of the study participants were male, the majority, 69.4%, were between 18-45 years of age with a mean age of 31.4 years. About 73% of study participants were on DOTS while 27% were registered to receive MDR-TB treatment. About 15.8% of TB patients on DOTS were co-infected with HIV while 26.3% MDR-TB patients had HIV co-infection. The assessment showed that 67.1 % TB patients to have BMI <18.5 kg/m² while 36% had BMI <15.3 kg/m². 74.6 % MDR-TB cases had BMI <18.5 kg/m² while 42.5% had BMI <15.3 kg/m². The assessment revealed that only 3% of TB patients and 26% of MDR-TB patient to have baseline nutritional assessment, and only 4.6% of TB patients on DOTS and 27.9 % of MDR-TB patients received some type of nutrition support in last one-month time.

Conclusion: Malnutrition is highly prevalent problem among both TB and MDR-TB patients in Ethiopia. Nutritional assessment counseling and support program is recommended to be integrated in the routine care of TB patients.

OA-428-28 Alcohol and substance use among participants in a clinical trial receiving home-based DOT for tuberculosis

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Background: Alcohol and substance use among patients with tuberculosis (TB) is commonly reported and may contribute to poor adherence and treatment outcomes. Often, patients with alcohol and/or substance use (ASU) are excluded from participation in clinical trials, despite being an epidemiologically important subgroup for TB control. To inform the feasibility of inclusion of TB patients with ASU in future trials, we describe the prevalence of ASU, time-to-treatment completion, extra visits necessary, and early terminations among participants participating in a Phase II clinical trial in Lima, Peru.

Methods: Data were reviewed from 180 participants who received treatment through community-based DOT for newly diagnosed, drug susceptible-TB in a clinical trial in Lima, Peru (2013-2015). Self-report of ASU was recorded at baseline by a clinical investigator. The number of days needed to complete treatment, number of unscheduled visits required, and number of early terminations were evaluated and compared between those who did and did not report ASU. The *t* test and χ^2 statistics were computed.

Results: Of the 180 trial participants, 89 (49%) self-reported ASU at baseline. Among all participants completing the 6-month treatment regimen (*n* = 146), average time to completion for those reporting ASU was 176 days (range: 170-226, SD 6.5), and 175 days (range 172-182, SD 1.8) for those with no reported ASU, (*P* = 0.24). Those reporting any ASU averaged 1.9 unscheduled visits, while those with no reported ASU averaged 0.9 (*P* = 0.02). Of the 34 early terminations, 19 reported any ASU while reported 15 no ASU (*P* = 0.40). Any reasons for the differences in the distribution of unscheduled visits will be reported.

Conclusions: Almost half of all participants self-reported ASU. This group completed more unscheduled study visits but did not, on average, take longer to complete treatment or have more early terminations than those reporting no use. Results suggest that, with additional support by the study team, participants reporting ASU may be candidates for inclusion in TB research. Inclusion of this sub-group, especially in Phase 3 trials, will allow results to be generalizable to larger populations with TB and ASU present.

19. Drugs for MRD-TB: challenges and successes

OA-429-28 Timing of acquired resistance to fluoroquinolones and second-line injectable drugs during treatment of MDR-TB

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Background: Acquired resistance to a fluoroquinolone (5.1%) or a second-line injectable drug (SLI, 2.9%), or both (1.1%) emerged in 9.1% of pulmonary MDR TB patients in a large, multinational prospective study, based on comparing phenotypic drug susceptibility test (DST) results of the first and last positive sputum cultures with matching genotypes. We have now completed DST for all monthly cultures for these patients to determine how soon acquired resistance emerges.

Methods: From January 2005 to December 2008 we enrolled 1761 consecutive consenting adults with locally confirmed pulmonary MDR-TB in 9 countries and followed them for 2 years or end of treatment with monthly sputum cultures. Duplicates of positive cultures were shipped to CDC. The first and last were tested for drug susceptibility by the proportion method on Middelbrook 7H10 agar. In case the DST results changed for isoniazid, rifampin, ciprofloxacin, ofloxacin, kanamycin, amikacin, or capreomycin, drugs considered to give reliable results, the paired isolates were genotyped by the 24-locus MIRU/VNTR method. For those with matching genotypes, all monthly isolates have now been tested for drug susceptibility. Time to acquired resistance was taken as the time from the start of treatment to the midpoint between the last susceptible isolate and the first resistant isolate.

Results: Of 164 patients with changing DST results and matching genotypes, 78 patients had serial isolates showing a clear-cut change from susceptible to resistant, including 57 who acquired fluoroquinolone resistance and 29 who acquired SLI resistance (8 acquired both). Fluoroquinolone resistance emerged in a median of 91 days (interquartile range [IQR] 56-198). SLI resistance emerged in a median of 116 to 136 days (IQR 65-251).

Conclusions: One-fourth of acquired resistance emerged in 7-8 weeks for FQ and 17-19 weeks for SLI. Median time-to-acquired resistance was 3 months for FQ and 4

months for SLI. One-fourth emerged after 6 months, while 10% was detected only after 15 months of treatment. Repeat DST is warranted if cultures remain positive after 2 or 3 months.

OA-430-28 Comparable 12-month incidence of renal insufficiency in MDR-TB patients treated with standard kanamycin-based regimens or concomitantly with tenofovir in Namibia

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Background: The anti-mycobacterial drug kanamycin (Km) and the antiretroviral drug tenofovir (TDF) are both nephrotoxic. We compared the incidence of renal insufficiency over 12 months among Namibian patients treated for multidrug-resistant TB (MDR-TB) with standard kanamycin-based MDR-TB regimens or concomitantly treated with TDF, for the human immunodeficiency virus (HIV).

Methods: We reviewed treatment and laboratory records of MDR-TB patients enrolled in care between January and December 2014. Using the LinkPlus® software, patient records in the MDR-TB, laboratory and the HIV treatment databases were electronically linked. Patients' estimated renal creatinine clearance (eGFR) values were calculated from serum creatinine levels using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation. Renal insufficiency was defined as eGFR of less than 60 ml/min. The standard MDR-TB regimens comprised of kanamycin (15 mg per kilogram body weight per day), cycloserine, ethionamide, levofloxacin and pyrazinamide, sometimes plus ethambutol. Mean eGFR values were compared before and after start of MDR-TB therapy and between the two treatment groups using the *t*-test at the 0.05 level of significance.

Results: In 2014, there were 157 patients registered in the MDR-TB treatment database who were tested for serum creatinine levels, with a mean age of 34.8 ± 12.9 years, predominantly male (62%); and 48% being HIV co-infected. All 157 patients were treated for MDR-TB with a Km-containing regimen (Km group), but 49 were additionally treated for HIV with a TDF-containing regimen (Km+TDF group). The mean baseline eGFR for the Km group (137.9 ml/min) and for the Km+TDF group (131.2 ml/min) were similar ($P = 0.15$). After 9-12 months, the mean eGFR values had significantly declined to 104.3 ml/min in the Km group, and to 103.4 ml/min in the Km+TDF group ($P < 0.001$). The two patient groups had a comparable incidence of renal insufficiency of 3.6 vs. 3.3 cases per 100 person-months, ($P = 0.78$).

Conclusions: Renal function declined at a similar rate in MDR-TB patients treated with standard kanamycin-based regimens compared to the MDR-TB-HIV co-

infected patients concomitantly treated with tenofovir-based antiretroviral regimens. Concomitant administration of TDF with Km does not appear to increase the risk of nephrotoxicity compared to Km alone after 9-12 months of treatment.

OA-431-28 Dose-ranging activity of clofazimine in combination with the first-line regimen in the mouse model of tuberculosis treatment

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Background: In the mouse model of tuberculosis (TB), clofazimine at 25 mg/kg has potent bactericidal and treatment-shortening activity when added to the first-line regimen, resulting in relapse-free cure after only 3 months of treatment. The objective of this study was to determine the lowest dose of clofazimine that, when added to the first-line regimen, resulted in relapse-free cure in three months.

Methods: *Mycobacterium tuberculosis* infected BALB/c mice were treated with one of the following regimens: no drug control; standard first-line regimen, 2RHZE/4RH (2 months of rifampin [R] 10 mg/kg, isoniazid [H] 10 mg/kg, pyrazinamide [Z] 150 mg/kg, and ethambutol [E] 100 mg/kg, followed by 4 months of RH); and five 4-month clofazimine-containing regimens, 2RHZEC/2RHC, in which the doses of clofazimine (C) were 25, 12.5, 6.25, 3.1, and 1.5 mg/kg. Lung CFU counts and relapse rates were assessed.

Results: The mean bacterial burden in the mouse lungs at the start of treatment was $7.11 \log_{10}$ CFU. After 2 months of treatment with RHZE, the mean lung \log_{10} CFU count was 3.18; after 2 months of treatment with the C-containing regimens, the mean \log_{10} CFU counts in the lungs were C dose-dependent, ranging from 3.06 (mice receiving 1.5 mg/kg) to 1.70 (mice receiving 25 mg/kg). After stopping administration of Z and E, mice receiving RH were all culture negative in the lungs after 5 months of treatment. Mice receiving RH plus C at 25 or 12.5 mg/kg were all culture negative after 3 months of treatment, and mice receiving RH plus C at 6.25 mg/kg were all culture negative after 4 months of treatment. Mice that received RH plus C at 3.1 or 1.5 mg/kg did not become culture negative after 4 months of treatment and had higher CFU counts in the lungs than the mice receiving the standard regimen without clofazimine.

Conclusions: In mice, clofazimine at 25 and 12.5 mg/kg equally contributed significant bactericidal activity to the first-line regimen, while clofazimine at 6.25 mg/kg was less potent and at 3.1 and 1.5 mg/kg was not contributing any bactericidal activity.

OA-432-28 Roll-out of new drugs to treat DR-TB: success and challenges with implementation

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Background and challenges to implementation: Bedaquiline (BDQ), a new drug developed to treat drug resistant tuberculosis (DR-TB), was added to the armamentarium of drugs used in South Africa in 2014 as part of a Bedaquiline Clinical Access Programme (BCAP). Following successful treatment outcomes observed in BCAP, BDQ was approved for routine use in South Africa. In June 2015 policy guidelines on the introduction of new drugs to treat DR-TB was published. In KwaZulu Natal, King Dinuzulu Hospital Complex, the centralized drug resistant tuberculosis centre was identified to roll out BDQ. Prior experience with BDQ was limited to 69 patients started in BCAP with the new target being 1000. The introduction of BDQ into the treatment regimen was viewed with mixed emotions as despite being a lifeline for patients, limited prescriber experience, challenges experienced during BCAP, human resource constraints and lack of systems threatened to erode perceived successes.

Intervention or response: A collaborative effort followed that included stakeholder involvement, the development of BDQ stationery to guide implementation and training of the interdisciplinary team. Pre-printed application forms, colour coded prescription charts and ADR reporting tools were developed and piloted prior to adoption. A unique tracking system consisting of T and BL numbers were implemented and a database of applications received and approved is maintained. Forecasting of the new drugs was informed by the application process and additional funding was sourced. **Results and lessons learnt:** As at 3 March 2016, 546 applications were received. Of the 546 applications 459 applications were approved either at facility, provincial or national level depending on the complexity of the cases. 386 patients started treatment as per Pharmacy register using the preprinted prescription charts. 11 patients died after starting treatment and 5 patients died before starting treatment. Some patients were awaiting treatment start for various reasons.

Conclusions and key recommendations: The translation of policy into practice requires collaboration with the interdisciplinary team to ensure that the right patient is selected for treatment and optimal monitoring is in place. Lessons learnt will be duplicated during the introduction of Delamanid into armamentarium against DR-TB.

OA-433-28 Treatment outcome in patients with multidrug-resistant tuberculosis as measured by sputum culture conversion rate in Rwanda

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Background: Sputum culture conversion at two months is considered as a predictor of successful treatment outcome in multidrug-resistant tuberculosis (MDR-TB). However, little is known about the time to sputum culture conversion in MDR-TB patients in developing countries like Rwanda. We describe time to and predictors of sputum culture conversion among MDR-TB patients in a Rwanda, a TB-endemic and resource-limited setting.

Methods: This is a retrospective, observational study of consecutive patients initiating the standard MDR-TB treatment between 1 January 2010 and 30 April 2014, period preceding the implementation of the short regime in Rwanda. Patients with culture-proven MDR-TB were treated with a standardized second-line regimen. Sputum cultures were taken monthly and time-to-conversion was measured from the day of initiation of MDR-TB therapy. Rate and predictors of culture conversion at two and six months were evaluated

Results: Among 244 MDR-TB patients, 203 (83%) and 225 (92%) culture-converted within the first two and six months respectively. Among the six patients who did not culture convert at the end of the treatment, one died, two were classified as treatment failure and 3 patients remained persistently culture-positive despite a clinically improved. High initial sputum culture colony count was associated with a delay in sputum culture conversion.

Conclusions: Rwanda has registered very good treatment outcomes among the MDR-TB patients with a high proportion of patients achieved culture conversion at two and six months reaching a treatment success rate of 89%. Further studies evaluating other clinical predictors of culture conversion are needed to help in better care of individual patients by identifying them early for aggressive treatment.

OA-434-28 Predictors of unfavourable treatment outcome in adults with multidrug-resistant tuberculosis in India

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Background: Global efforts to control tuberculosis (TB) are now being hampered by the emergence of drug

resistant TB which is a major concern for TB control programs worldwide. Treatment of multidrug-resistant (MDR) TB requires prolonged use of multiple anti-TB drugs that are less efficacious, costly and associated with more adverse events. As a consequence, the outcomes in MDR-TB are significantly worse. There are very few reports from India on the treatment outcomes in MDR-TB patients. There is insufficient information on the socio-demographic and clinical factors associated with unfavorable outcomes. The aim of this study was to describe the programme defined treatment outcomes in MDR-TB and to determine various factors associated with unfavourable treatment outcomes.

Methods: A retrospective cohort analysis of MDR-TB patients initiated on treatment under Revised National TB Control Programme in Delhi, West Bengal and Kerala from January 2009 to December 2011 was done. The sources of data were the treatment cards and registers. The programmatic definitions were used for treatment outcomes. Multivariate analysis was done to identify independent predictors of unfavorable treatment outcomes.

Results: Among the 780 MDR-TB patients, who had documented treatment outcomes, 469 (60%) had a favorable outcome [cure 393 (84%); completed treatment 76 (16%)]. Of those with unfavorable outcome, 135 (43%) died, 128 (41%) defaulted, 43 (14%) remained culture positive at the end of treatment. Two patients were switched to treatment regimen for extensively drug resistant TB. The adjusted multivariable logistic regression analysis showed that a delayed sputum culture conversion of > 9 months (aOR 5.4, $P = 0.013$) and treatment interruptions of more than a month during Intensive phase (aOR 1.93, $P = 0.003$) are associated with unfavourable treatment outcomes.

Conclusion: A better understanding of factors influencing treatment outcomes among MDR-TB patients is necessary for the programme to provide appropriate case management and effective interventions. Efforts must be multifaceted to address these risks. Interventions are required to improve the diagnostic approaches as well as adherence and should target the specific risk groups.

OA-435-28 DR-TB treatment costs: trends towards more affordability under threat with new drugs

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Background: Patients with drug-resistant tuberculosis (DR-TB) often do not have access to appropriate treatment. The World Health Organization estimates that only half of patients with multidrug-resistant tuberculosis (MDR-TB) were successfully treated and cured in 2014. One of the limiting factors to scale up is the cost of treatment, of which cost of drugs is a major factor.

Methods: MSF sent questionnaires to companies that were listed on the Global Fund List of Tuberculosis Pharmaceutical Products. The companies all produce at least one anti-tuberculosis drug found on the WHO list of prequalified medicinal products or approved by a stringent regulatory authority (SRA) or temporarily approved by the Expert Review Panel (ERP) of the Global Fund. Data was collected from August to September 2015 and not all manufacturers agreed to share information. Some companies did not wish to contribute to the publication and others did not have prices available or were unwilling to publish prices. Prices are given in US dollars according to the lowest unit price and may be higher or lower for actual purchasers due to factors such as import taxes.

Results: Recent price decreases for DR-TB drugs have resulted in the reduction of the cost of preferred regimens down to a range of US \$1800-\$4600 per treatment course (excluding Group 5 and new drugs). This range represents a significant improvement compared to prices seen in 2011: US \$4400-\$9000 per patient for a standard 18-24 month treatment course. Competition from generic manufacturers has lowered prices for linezolid, capreomycin, and levofloxacin and cycloserine has become increasingly affordable due to more manufacturers of active pharmaceutical ingredients. Prices have not changed for clofazimine, amikacin, prothionamide, and ethionamide and have increased for Kanamycin and PAS-sodium. Treatment courses for bedaquiline (tiered pricing for countries excluded from donation) and delamanid (US \$1700) remain costly.

Conclusions: While prices have decreased for DR-TB regimens they remain as much as US \$4600 per treatment course, and therefore remain unaffordable. Pharmaceutical companies should offer affordable, sustainable prices, not limited to countries' income tiers, and countries should capitalize on public health exceptions in international intellectual property law and promote competition.

OA-436-28 High rates of ocular toxicity associated with ethambutol in the treatment of multidrug-resistant tuberculosis in South Africa

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Background: Ethambutol (EMB) is a well-tolerated first-line drug often used in multidrug-resistant tuberculosis (MDR-TB) treatment regimens. Although EMB-related ocular toxicity has been documented in drug-susceptible TB treatment, little data are available among MDR-TB patients, who are typically prescribed EMB at higher doses and for up to 24 months. Additionally, there are no

data in African patients and in the setting of HIV co-infection.

Methods: We assessed loss of color discrimination, an early symptom of ocular toxicity, using Ishihara plates in a prospective cohort of MDR-TB patients with and without HIV co-infection. Patients were enrolled upon initiation of a standardized MDR-TB treatment regimen, which included EMB, and followed until treatment completion. Color discrimination testing was done at baseline, every 2 months during the intensive phase, at 12 months, and 24 months. Reduction in color discrimination was defined as scoring lower than at baseline. Regaining color discrimination was defined as any improvement in score up to 24 months after the start of treatment.

Results: We enrolled 189 (137 HIV-infected, 52 HIV-negative) participants with MDR-TB who were prescribed EMB. Dosages ranged from 10.3 mg/kg to 25.5 mg/kg (mean 20.1 mg/kg, SD 3.6). 185 patients underwent an average of 4 (SD 1.45) color discrimination tests, with a median of 12 months (IQR 5-24) between first and last test. 19% (25/134) of HIV-positive and 10% (5/51) of HIV-negative patients had diminished color discrimination during MDR-TB treatment, the majority (73%; 22/30) of whom showed diminished ability within the first 3 months of treatment. 60% of HIV-positive (15/25) and HIV-negative (3/5) patients regained some color discrimination ability over the course of treatment, while the remaining 40% (12/30) did not. There was no significant difference in vision loss patterns by HIV status ($P = 0.28$).

Conclusions: This is one of the first estimates of vision loss during MDR-TB treatment and in the setting of HIV co-infection. A substantial proportion of patients receiving EMB-containing regimens experienced loss of color discrimination and did not recover vision during treatment. Further research that includes post-treatment vision monitoring and use of additional tests of visual acuity is needed to more thoroughly examine EMB-related vision loss.

20. TB infection control: too fast, too slow or just right?

OA-437-28 Shortening time to diagnosis and treatment initiation for infectious TB and drug-resistant TB cases by implementation of FAST in Viet Nam

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Background: Hospital without effective infection control measures can become place to facilitate nosocomial transmission of TB and MDR-TB. The USAID's TB CARE II Project in collaboration with the National TB Program introduced FAST - a new strategy to early detect, diagnose, and initiate effective treatment of

infectious TB cases - at Quang Nam Provincial Hospital of TB and Lung Diseases in Viet Nam, a country with high TB and MDR-TB burden.

Methods: Between May 2014 and December 2015, Quang Nam hospital implemented key FAST activities including improved screening of patients using a standardized patient information form to quickly detect presumptive TB and MDR-TB cases, requesting appropriate diagnostic tests, and early initiating effective regimens. The patient information form captured patients' hospitalization history, previous TB treatment, exposure and TB related tests from referring facilities. Presumptive TB cases with TB suspecting x-ray and presumptive MDR-TB cases were prioritized for Xpert testing, which had been available on site since October 2013. Sputum smears and X-ray were first requested for other presumptive TB cases. The Project continuously trained relevant staff and supported recording and reporting tools to aggregate and analyze data for routine monitoring.

Results: The number of pulmonary TB cases with positive smears rose from 214 to 273 in the periods of May-December 2014 and January-December 2015 with 4 days as the average time from patient visit to treatment initiation. In the same periods, the number of smear-negative pulmonary TB cases diagnosed with Xpert rose from 153 to 360 while the average number of days from the patient visit to treatment initiation was reduced from 9.5 to 7.5. This time indicator was reduced from 9.7 to 7.3 days for 29 and 25 MDR-TB cases diagnosed in May-December 2014 and January-December 2015, respectively. The average number of days from receipt of Xpert specimens to MDR-TB treatment initiation fell from 10.6 in January-April 2014 to 6.4 in May-December 2014 and to 5.6 in January-December 2015.

Conclusions: FAST approach successfully increased the number of bacteriologically confirmed pulmonary TB and drug-resistant TB cases and decreased time to diagnosis and treatment initiation, thus reducing transmission of TB infection at the selected setting.

OA-438-28 FAST: a new strategy for TB infection control

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Background and challenges to implementation: Non presumptive or undiagnosed TB and/or MDR-TB cases are the main source of TB/MDR-TB infection. FAST is a novel infection control strategy with a focused approach to stopping TB spread in congregate settings by early diagnosis of TB/MDR-TB those who are not even counted as presumptive. In English, FAST stands for Finding TB cases Actively, Separating safely, and Treating effectively.

Intervention or response: The FAST strategy was introduced at the National Institutes for Disease of the Chest and Hospitals (NIDCH) in Dhaka, Bangladesh, in 2013. Later it was scaled up to the Bangladesh Institute

of Research & Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM) in Dhaka and to the Chittagong Chest Disease Hospital. Sputum of all newly admitted cases in those three facilities were tested by GeneXpert. The patients were divided into two groups. One group contained TB patients but not known MDR, to screen the MDR cases and another group was 'Other lung disease' but not known TB case to screen for TB / MDR TB cases.

Results and lessons learnt: From January 2014 to June 2015, a total of 6710 patients have been actively screened utilizing the FAST strategy. From these patients, 733 (10.92%) and 89 (1.33%) were identified as non-presumptive TB and MDR-TB cases respectively. Therefore, a total of 822 (12%) in-coming patients who would not have previously been identified or would have been delayed in being diagnosed as TB and MDR-TB patients were diagnosed and initiated on therapy for TB or MDR-TB.

Conclusions and key recommendations: The implementation of the FAST strategy to date has demonstrated some key lessons, namely that: Minimal systemic alterations to practices around diagnosing and treating patients, such as ward registers and laboratory tracking tools, can greatly expedite and improve patient care. Through simple facility-based policy changes, non-presumptive TB and MDR-TB patients were identified and put on effective therapy, thereby potentially limiting the amount of infectious agents present in the healthcare facility.

OA-439-28 Comparison of indoor contacts in Zambia and South Africa suggests infection control intervention targeting should be informed by local data

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Background: In high incidence settings, the majority of *Mycobacterium tuberculosis* transmission occurs outside the household. Little is known about where people's indoor contacts occur outside the household, and how this differs between settings. We estimate the number of contact hours that occur between adults and adult/youths and children in different building types in urban areas in Western Cape, South Africa, and Zambia.

Methods: Data were collected from 3206 adults using a cross-sectional survey on buildings visited in a 24-hour period, including building function, visit duration, and number of adults/youths and children (5-12 years) present. The mean numbers of contact hours per day by building function were calculated.

Results: Adults in Western Cape were more likely to visit workplaces, and less likely to visit shops and churches than adults in Zambia. Adults in Western Cape spent longer per visit in other homes and workplaces than adults in Zambia. Overall numbers of adult/youth indoor contact hours were the same at both sites (35.4 and 37.6 hours in Western Cape and Zambia respectively, $P=0.4$). Child contact hours were higher in Zambia (16.0 vs. 13.7 hours, $P=0.03$). Adult/youth and child contact hours were highest in workplaces in Western Cape and churches in Zambia. Compared to Zambia, adult contact hours in Western Cape were higher in workplaces (15.2 vs. 8.0 hours, $P=0.004$), and lower in churches (3.7 vs. 8.6 hours, $P=0.002$). Child contact hours were higher in other peoples' homes (2.8 vs. 1.6 hours, $P=0.03$) and workplaces (4.9 vs. 2.1 hours, $P=0.003$), and lower in churches (2.5 vs. 6.2, $P=0.004$) and schools (0.4 vs. 1.5, $P=0.01$).

Conclusions: Patterns of indoor contact between adults and adults/youths and children differ between different sites in high *M. tuberculosis* incidence areas. Targeting public buildings with interventions to reduce *M. tuberculosis* transmission (e.g. increasing ventilation or UV irradiation) should be informed by local data.

OA-440-28 TB infection control assessment at high-burden antiretroviral therapy centres under the Three I's project in India: country experience

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Background and challenges to implementation: Tuberculosis is commonest opportunistic infection and leading cause of morbidity among People living with HIV. There is the risk of transmission of tuberculosis infection occurring in health care facilities especially when patients remain undiagnosed and untreated for tuberculosis. Outbreaks reported in different countries and high mortality among People Living With HIV (PLHIV) have reemphasized the need for strengthening TB infection control in health-care facilities especially HIV and TB care facilities. The National Airborne infection control (AIC) guidelines and National Framework for HIV TB in India emphasise TB infection control in all HIV TB settings, still there is a practice gap in implementing AIC measures.

Intervention or response: Advocacy, Sensitisation of National level program managers and Training of State level officers was conducted. Anti-Retroviral Therapy (ART) centres assessment tool was developed and monitoring indicators for airborne infection control were developed. Under the Innovative Three I's (Intensified case finding, Isoniazid Preventive Therapy, Infection control), 30 high burden ART centres in five states

in India, were selected. A team trained in the AIC assessment conducted baseline assessment using the standardised tool and equipment's for assessment during October to December 2015. Qualitative and Quantitative data was compiled and collected and observations and recommendations were provided to each of the 30 sites.

Results and lessons learnt: Findings baseline assessment of ART centres suggest need for strengthening administrative, environmental and respiratory protection measures. Majority of ART centres had limited space, with overcrowded waiting, outpatient areas and patient mixing with general health facility. Health care workers surveillance was not happening regularly and limited availability of N95 respirators was evident. Summary findings are shown in the Table.

Conclusions and key recommendations: There is critical need of strengthening of AIC measures at HIV-TB settings with novel approach of assessment of ART centres and sustainable funding support for airborne infection control activities implementation.

Figure Summary results of AIC assessment at ART centres

Indicators	Y	%
Facility level infection control (IC) committee or bio-medical waste (BMW) management	22	73
Is the ART center Nodal Officer a member of the HCCC?	16	53
Facility IC/BMW management plan available in written form?	11	37
Is there an institutional policy to provide N-95 or FFP2 (or higher) respirators to staff who	5	17
Is a site-specific "facility infection control plan" including AIC been developed and is available to staff at ART center?	0	0
Has a facility risk assessment for AIC been performed at least annually?	1	3
Is infection control education/training for staff been performed in last 2 years?	11	37
Are patients with cough or other symptoms of TB promptly separated and fast tracked?	22	73
Are signages for cough etiquette displayed?	15	50
Does the Care Coordinator does routine ICF for all clients with any of the four symptoms	20	67
Is the fast tracking of cases also done at other services such as pharmacy, laboratory etc.	14	47
Are tissues, masks, bins etc available for coughing patients?	9	30
Are TB AIC practices monitored daily	6	20
Is Disease Surveillance in HCWs is a part of the facility IC/BMW plan?	2	7
Is active screening for TB done for ART staff?	1	3
Does the facility design, patient flow and triage system comply with what is outlined in the infection control plan and/ or national infection control policy?	9	30
Is the waiting area well ventilated (i.e. windows and doors open when feasible) and there	12	40
Are patients crowded in hallways or waiting areas?	18	60
Are sputum samples collected in a well-ventilated, clearly designated area away from	17	57
If Ultra Violet lighting is used are routine cleaning and maintenance conducted and	9	30
Are surgical masks available for patients with cough or other TB symptoms?	14	47
Are N-95 or FFP2 (or Higher) respirators readily available to all staff that have contact with patients with TB or suspected of having TB in the center?	4	13
Are staffs trained on proper fit of respirators and documentation of training is available?	0	0

OA-441-28 Infection control in MDR decentralised sites in South Africa: a baseline study

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Background: South Africa's MDR-TB burden ranks third highest in the world with the highest number of people living with HIV. Prior to 2011, national policy mandated that all DR-TB patients be initiated on treatment in specialized TB hospitals. New cases outstripped the bed capacity and the country had to move to the decentral-

ized approach with the intention of bring MDR-TB treatment closer to the community. Infection Control (IC) is one of the requirements for decentralised MDR - TB care. The objective of the study was to determine infection control needs and priorities for improving MDR-TB care in South African health care facilities.

Methods: A cross-sectional descriptive study of 128 decentralized MDR-TB facilities (10 MDR-TB/TB Hospitals, 52 hospitals and 66 Primary Health Care clinics/Community Health Centers) was conducted from October 2014 to February 2016 using a standard assessment instrument comprising of the following: availability of IC guidelines, IC committee/meetings, safe sputum collection area, infection control plan, well ventilated waiting areas, patients screening/triage, fit testing and availability of N95 respirators and infection control training done. Fifty-three of 128 (41%) facilities were providing MDR-TB services at the time of assessment. Key informants were interviewed and hospital walkabout conducted. Following the initial assessments, infection control plans were developed to help them attain the minimum requirements to support decentralization.

Results: The assessment revealed infection control challenges/deficiencies which varied between the 128 facilities. Most sites (92%) had access to the recent infection control guidelines, 50% do screening, but a limited number of facilities (20%) had infection control committees, infection control plans (25%) and IC officers (25%). Only 30% have safe sputum collection points and only 10% indicated that they had IC assessments done. Patient screening was done at 20% of the facilities and 80% of facilities do have N95 respirators although it was not visible at all facilities

Conclusions: These findings demonstrate a clear need to improve and standardize IC practices in identified decentralized MDR-TB settings. Infection controls varied between facilities.

OA-442-28 Exploring level of knowledge of health care staff on TB infection control measures in Afghanistan

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Background and challenges to implementation: Hospital acquired infections are a major public health problem in Afghanistan and their prevention has been made a priority by the WHO. The aim of the assessment was to better understand the barriers and help guide optimal implementation of infection control practices (ICPs) in 80 of 205 health facilities; we wanted to gather baseline information regarding ICPs.

Intervention or response: Challenge TB and National Tuberculosis Program (NTP) implemented a cross sectional baseline evaluation of health care workers'

knowledge, attitudes and practices of tuberculosis (TB) infection control and hand hygiene (HH) between January-February 2016 at 80 health facilities in 15 provinces. A standardized questionnaire was administered to health care workers (HCWs). Knowledge items were scored as correct/incorrect. Attitudes and practice items were rated from 5 to 3 points rating scales. Descriptive statistics were used to assess responses.

Results and lessons learnt: 230 surveys were completed by nurses (40%), physicians (35%), and laboratory technicians (25%). 70% were male. 26% of HCWs did not believe HH was necessary before patient contact. HH practices were variable, only 7% of HCWs reported regularly performing HH prior to patient contact while 49% reported performing HH after patient contact. Barriers to HH included lack of soap and running water (76%). TB infection control (IC) knowledge was excellent among HCWs (>90% correct. Most HCWs agreed that they were at high risk of acquiring TB from patients (71%) that TB IC can prevent TB transmission within their hospitals (92%), and that TB IC is important to protect patients (95%). Only 15% of HCWs regularly wore respirators when carrying for TB patients. Limited access to masks and poor design of HF's building to isolate infectious TB patients and maximize ventilation were the only limitations of TB IC. Half of HCWs felt UV lights may be harmful.

Conclusions and key recommendations: Raising awareness among HCWs about the importance and proper practice of HH along with providing hand antiseptic soap may help improve patient safety. Additionally improved infrastructure is needed to improve TB IC and allay HCWs concerns of acquiring TB in hospitals.

OA-443-28 Assessing tuberculosis patients' knowledge, attitudes and practices: research to strengthen infection control interventions in PHC facilities in South Africa

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Background: Apart from providing care, treatment and cure, health care settings also expose both patients and healthcare workers, especially those with immunosuppression, to tuberculosis (TB) infection. The objective of this research was to assess the TB and Infection control (IC)-related knowledge, attitudes and practices of patients attending state-run PHC facilities in the Mangaung Metropolitan of the Free State.

Design/Methods: In 2015, a facility-based cross-sectional study was conducted among TB and general patients attending PHC facilities in the Metropolitan. Probability proportional-to-size sampling was used to select patients across 40 facilities. Data was collected through interviews with patients. Data on patients' demographics and knowledge, attitudes and practices regarding TB was subjected to descriptive and inferential statistical analyses using SPSS (version 23).

Results: A total of 511 patients (median age 38; IQR 29-48) were interviewed. Three in every five ($n = 324$, 63.4%) respondents were female, two in every five ($n = 215$, 42.1%) were TB patients, and the majority ($n = 363$, 71.0%) attended clinics in more centrally located urban areas. More than half (60.7%, $n = 310$) of the patients reported having received TB prevention information from the clinic. TB knowledge scores were not statistically different between general and TB patients [$t_{(498)} = -1.056$, $p = 0.291$]. Provision of TB information at clinics significantly improved patients' self-reported attitudes towards TB [$t_{(358.2)} = 2.674$, $P < 0.01$]. Significantly more positive attitudes regarding TB disease and prevention were observed among patients attending clinics in remote black settlement areas [$F_{(2, 327)} = 9.723$, $P < 0.001$] relative to those attending clinics closer to the city center. Provision of TB information also significantly improved self-reported infection control practices [$t_{(345)} = -2.801$, $P < 0.01$]. Good cough etiquette (24.5%) was the most cited precaution taken against TB in clinics.

Conclusions: The results confirm that dissemination of TB information improves patients' attitudes and practices towards TB prevention. The results are useful for the development of more effective TB prevention interventions and management practices. Particularly, health education should be strengthened to assist in enforcing TB infection control, especially in PHC clinics close to the city center.

OA-444-28 Incidence of tuberculosis among health workers at public health care facilities in two regions of Ethiopia

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Background: Surveillance of tuberculosis (TB) among health workers (HW) is not a standard practice in most settings. Our objectives were to investigate the implementation of HW TB screening at public health care facilities (HF) and the TB incidence rate amongst HWs.

Methods: A cross sectional study was conducted in all the 60 hospitals in the Amhara and Oromia regions and 11 high patient load health centers. Data was collected via structured questionnaire. The number of HW who had TB disease during the past year (2013/14) was obtained. HW included all clinical and administrative staffs salaried in the health facility.

Results: At least one case of TB disease among HW was reported in 40.8% (29/71) of the HF (all being hospitals) with a total of 70 TB cases in one year. All HW who had TB were treated as per the national guideline. A maximum of eight TB cases were reported in two hospitals. The incidence rate of all forms of TB cases in the 29 hospitals that reported cases was 885.1 per 100 000 per year (Table) whereas the incidence rate in all 71 health facilities was 460.3 per 100 000 per year. The incidence rate computed per health facility population

ranged between 330 and 3278.7 per 100 000 per year. Regular symptomatic screening of health workers on TB was conducted by only one (1.4%) health facility. The TB case notification in the general population in the two regions in 2013/14 was reported to be 135.3 per 100 000. **Conclusion:** The incidence rate ratio was found to be 6.5 in reference to the TB case notification in the general population. A routine screening system and medical check-up is recommended to estimate the burden of TB in health workers, monitor trends and implement TB infection control measures to decrease nosocomial transmission.

Table Number of incident TB cases diagnosed in health workers

Number of TB cases in HWs per year	Number of hospitals	Total number of TB cases	Number of HWs	Incidence rate per 100 000/year
1-4	26	48	6295	762.5
6	1	6	201	2985.1
8	2	16	1413	1132.3
Total	29	70	7909	885.1

POSTER DISCUSSION SESSIONS

20. 'Help!' Identifying TB education and training needs and outcomes from selected interventions

PD-802-28 Tuberculosis knowledge, attitudes and practice among cases and contacts in a UK city

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Background: Culturally-competent health services are important to engage the communities affected by disease. Assessing knowledge, attitude and practice (KAP) of health users can help identify gaps in service provision and improve program planning. Data from low-burden tuberculosis countries are scarce.

Methods: We administered a KAP questionnaire to 100 randomly selected TB patients and/or TB contacts in Birmingham, UK who had been in contact with the TB service in the preceding 12 months. The majority of survey questions were structured and pre-coded to explore perception of the severity of TB, awareness of TB symptoms and transmission routes, types and preferences of information sources and satisfaction with services provided.

Results: Median age of participants was 30 years, 48% were UK-born and 46% had at least post-secondary education. Fifty-two per cent considered TB a very serious problem in the community and 82% could name at least one TB symptom. 65% understood the route of TB transmission and 23% had different perceived risks

of transmission when exposed to household vs. non-household TB cases. Thirty per cent would not worry if they were diagnosed with TB. Eighty per cent wished they had more information about TB. The main sources of information used were the internet (39%), healthcare workers (28%) and TB leaflets or posters (12%). Participants perceived a high level of TB stigma in the community with over 50% strongly agreeing or agreeing that TB patients lost friends, were a burden to their family and were treated differently to other community members.

Conclusions: Levels of TB understanding were moderate and could be improved. Interventions to address TB-related stigma is urgently needed in our setting.

PD-803-28 TB patient's existing and preferred sources of TB-related information: findings from a KAP survey across 30 districts in India

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Background: Health information that is scientific and evidence-based is important not only for policy makers but also to the community member and the end beneficiary. Providing easy to understand information on tuberculosis (TB) to general public and TB patients will empower them and aid in TB care and prevention. Knowing the TB patients' preferred source of information is an important aspect for developing advocacy and communication strategies.

Method: A cross-sectional knowledge attitude and practice (KAP) survey was conducted in 2013 across 30 districts in India. 10 primary sampling units were selected from each district and a household line listing process was used to identify TB patients. Identified patients were then interviewed using a pilot tested semi-structured questionnaire.

Results: A total of 496 self-reported TB patients were identified, of which majority were male (61%) and about 44% were illiterate. The most common source of health related information is television (50%) and hospital/doctor (45%). When asked about their sources for information regarding TB, 59% suggested that hospital or a doctor were the key source followed by television (48%) and friends or relatives (35%). Interestingly, patients prefer to get TB related information from hospitals or doctors (67%) firstly, followed by the television (52%), newspaper/magazines (29%) and friends/relatives (28%). The most-trusted source of information is health staff. The main information they received regarding TB was about symptoms and all other aspects is very limited.

Conclusion: Personal talk with qualified people is most preferred. Health staff have a great responsibility to share the TB-related information, as they are the most preferred and trusted source. However, it is not feasible to give time to each patient. Hence alternate strategies like awareness camps, health debates, discussions at village fairs etc. can be utilised by involving local health

staff. TB aspects like symptoms, treatment, cough etiquette, treatment adherence, spitting habits, when does a patient turn non-infectious, protecting children in the family, watching their diet, protecting self from tobacco smoke or indoor air pollution, dealing with the myths and others need to be communicated clearly and reiterated often for behaviour change.

PD-804-28 Operational research on the role of patient education in treatment outcomes

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Background: Only 55% of tuberculosis (TB) patients in Ukraine have a successful directly observed treatment short course (DOTS) cure rate, compared with the WHO standard of 85%. In 2014, according to the Ukrainian Center of Diseases Control, the effective TB cure rate in the city of Kyiv was 31%. It is well documented that one of the reasons for such a low cure rate and problems with treatment adherence has been the lack of knowledge among TB patients about the disease.

Methods: In 2015, the International HIV/AIDS and TB Institute, through support from the USAID Strengthening Tuberculosis Control in Ukraine (STbCU) project, conducted operational research (OR) in five selected primary health care facilities and TB clinics in Kyiv city. The purpose of the research was to examine the role of patient education in treatment outcomes and to analyze opportunities to improve patient education. The hypothesis was based on the premise that patient education, alongside tools for self-observation, will increase awareness of the risks and possible negative outcomes of TB. The OR phase included a desk review of legislation and best practices in patients' education; 15 interviews with the health care professionals and social workers; and 61 questionnaire-surveys from TB patients in the ambulatory phase of DOTS.

Results: OR showed that patients who were less informed about TB issues were more likely to miss treatment; 34.4% of TB patients show a low level of knowledge on TB; high adherence shows only 36.4% of patients with high levels of knowledge about tuberculosis. Patient surveys identified three sources of information as most useful: doctor (100%), nurse (52.5%) and informational materials (24.6%). Furthermore, one-third of patients indicated a need for information on the treatment of depression.

Conclusions: The hypothesis of this OR is confirmed. A large proportion of patients, particularly those belonging to socially vulnerable groups, need to have psychological support in combination with TB education. Medical professionals and social workers are ready to educate patients; however, they need to be trained and have standardized approaches for patient education.

PD-805-28 Tuberculosis prevention and control: how knowledgeable are hospital workers in India?

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Background: Each year 12 lakh (1 200 000) Indians are notified (that is reported to the RNTCP) as having newly diagnosed TB. In addition at least 2.7 lakh (270 000) Indians die. Some estimates calculate the deaths as being twice as high. Case notification is estimated to be only 58%. Over one third of cases are not diagnosed, or they are diagnosed but not treated, or they are diagnosed and treated but not notified to the RNTCP. This could be even higher, and the WHO (World Health Organization) estimates that another 10 lakh (1 000 000) Indians with TB are not notified. Healthcare workers have an increased risk of latent tuberculosis infection (LTBI), but previous studies suggested that they might be reluctant to accept preventive tuberculosis (TB) treatment. However, TB prevention and control in work places remained largely an uncharted area. This study was aimed to assess the hospital workers' current knowledge, attitudes and practices (KAP) on pulmonary TB which is essential for designing a TB prevention and control programme in the workplaces.

Methods: A cross-sectional survey was done in doctors and nurses among hospitals in Mangalore, South India using a random sampling procedure. Data on workers' KAP related to pulmonary TB were collected from 1290 hospital workers in face-to-face interview.

Results: Knowledge about symptoms was high (78.5%) and drug treatment (96%), but possessed limited knowledge regarding causation among nurses (24%) and mode of transmission (22%). Very few nurses 18% knew about preventive measures, e.g., taking BCG vaccine and/or refraining from spitting here and there. (64%) were aware about the treatment duration and consequences of incomplete treatment (21%). Majority of the workers were afraid of the disease, few of them felt embarrassed (and less dignified) if they would have TB, and 68% were afraid of isolation if neighbours would come to know about it.

Conclusions: The hospital workers had inadequate knowledge regarding its causation, transmission and prevention which may interfere with appropriate treatment-seeking for chronic cough including sputum test. Hospital staff in general had positive attitudes towards preventive TB treatment.

PD-806-28 Establishing a framework for TB nursing education in Australia

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Nurses comprise the largest proportion of the Australian TB Control Programme workforce. There are approximately 200 nurses directly engaged within the Australian TB Programme. Additionally, the TB Programme is

supported by other nursing staff employed in both inpatient and outpatients settings within the following related health fields: paediatrics, respiratory health, refugee health, community and public health. Australia has been identified by the WHO as one of 30 countries who could progress to a TB pre-elimination phase utilising eight key interventions to move towards pre-elimination and eventually, elimination. Intensified efforts to move Australia towards TB elimination will demand the involvement of a skilled and knowledgeable health care workforce. Nurses will play an important role in these efforts.

There is currently no dedicated TB specific education or training program available for nurses in Australia. In 2015, the Australian Respiratory Council funded a project to establish a national framework for TB nurses education. This work resulted in the first comprehensive description of the Australian TB nursing workforce, including a survey on workforce training needs and a review of current national and international educational courses available for TB nurses and other niche nursing specialities.

The project confirmed that there is strong interest and support for the establishment of a post graduate education pathway for TB nurses in Australia and identified interest in exploring how this may also be applied regionally and internationally. On the basis of these findings, work is currently being undertaken to identify potential training providers and collaborators including Universities, the WHO (Western Pacific Region Office) and The Union to establish a post graduate education pathway that is available to Australian TB nurses. In the interests of course sustainability and the development of regional capacity, opportunities for access to such a course by other TB nurses in the Asia Pacific Region or internationally is also being explored.

PD-807-28 A study of knowledge, attitudes and practice regarding *Mycobacterium tuberculosis* among private practitioners in Abbottabad District, Khyber Pakhtunkhwa, Pakistan

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Background: *Mycobacterium tuberculosis* is a serious public health issue globally and especially in developing countries like Pakistan. According to World Health Organization (WHO), Pakistan ranks fifth in high burden countries for *M. tuberculosis*, where approximately 420 000 new patients are diagnosed each year and half of these are sputum smear positive. The annual incidence of *M. tuberculosis* in Pakistan is between 180-270/100 000 people. The majority of *M. tuberculosis* patients consult private practitioners for initial diagnosis and treatment of TB. Knowledge and attitude of private practitioners regarding the diagnosis and treatment of TB is essential to assess. Several national and international studies have shown unsatisfactory knowledge of private practitioners regarding *M. tuberculosis* which leads to delay in the diagnosis and treatment of *M. tuberculosis*.

Therefore, the aim of this study was to assess knowledge, attitude and practice of private medical practitioners regarding the diagnosis and treatment of *M. tuberculosis* as per guidelines of WHO and NTCP in Pakistan.

Method: A cross-sectional study was conducted from November 2015 to December 2015, in Abbottabad district, Khyber Pakhtunkhwa, Pakistan, amongs 120 private practitioners who treat TB patients, using a self-administered semi-structured questionnaire.

Results: A total of 120 private medical practitioners were included in the study. Of the total 75 (62.5%) were males with mean age 45.4 +18 and 45 (37.5%) were females with mean age 39.6 +14. The difference between males and females in level of education was statistically significant; it was found that male doctors have more post graduation as compared to females ($P = 0.001$). About 58.5% replied that they advised ESR, chest X-ray, blood CP and with sputum smear test. About 63.5 % male and 45.8 % female replied correctly about the proper dosage of anti-tuberculosis drugs. Only, 35.5 % replied correctly about the follow up of TB patients. Similarly, only 25.8% replied correctly how to treat multidrug-resistant TB.

Conclusions: Results in this study showed that knowledge of private practitioners regarding the diagnosis and treatment of TB is unsatisfactory. Prescription behaviour of private practitioners is not standardized and contained some unnecessary medicines, which is an economic burden on patients. Therefore, private practitioners should be trained periodically.

PD-808-28 Building an educational campaign with the participation of the prison community

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Background and challenges to implementation: Tuberculosis is a serious public health problem in Brazilian prisons. Of 70 000 cases diagnosed every year in Brazil, 7.6% come from the prison population. Recognizing this population as a priority, the National Tuberculosis Program (NTP) submitted a project to TB Reach, a fund linked to the Stop TB Partnership, in 2013. The project had the objective to detect TB cases in three prisons, combining innovative strategies for Communication, Advocacy and Social Mobilization (CASM). This abstract describes the application of Focus Groups (FG) within the prison community.

Intervention or response: From August to October 2015, FGs were applied to inmates, health and security professionals and NGOs that work in the prisons. Lots of doubts, myths and prejudices related to TB were identified and the best strategies to the detection, diagnostic and treatment of TB were discussed.

Results and lessons learnt: Four FGs were applied, with the first composed by 25 inmates, and the rest with, at least, eight representatives of each public. The assessment pointed out the existence of lots of doubts about the

disease. Frequently, the scientific information gets mixed with the common sense. It was evaluated that the way the diagnostic and treatment of TB is conducted in the prisons contributes to a low treatment adherence, and to the dissemination of the stigma and prejudice. Moreover, the life conditions in these institutions, with the overcrowding, low ventilation and the lack of sun light are not favorable to the interruption of the transmission chain of the disease.

Conclusions and key recommendations: Through the FGs it was possible to identify which information the educational campaign should have, considering the specifics of each group for the content approach and the choice of the communication methodology and language. In addition, the assessment indicated the need to elaborate educational materials adequate to the reality of the prison system. It is necessary to innovate on how the information about TB are disseminated, expanding the participation of these populations in the creation process and sensitizing all the prison community about the importance of the topic.

PD-809-28 Improving the treatment success rate and case notification of smear-positive tuberculosis patients through household health education in Kenya

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Background: Tuberculosis (TB) remains a public health challenge post-2015 in developing countries. Kenya's notified TB cases dropped from 99 159 in 2012 to 89 760 in 2013 (9.48% decline) with a treatment success rate of 85% and positivity rate of 43.6%. In 2014, Kenya registered 34 997 (39%) pulmonary bacteriologically confirmed TB cases against a total of 89 294 notified cases lower than 45.4% ($n=8190$) registered in Kakamega, Kisumu and Machakos counties. These patients are known to be infectious and treatment and investigation of their contacts is key. In response to this, the Kenyan government has involved the public, private and Civil Society Organizations (CSOs) in implementing TB control activities. Amref Health Africa in Kenya, a non-state principal recipient, implemented the Global Fund TB Grants through 16 CSOs three of which implemented in the above 3 counties.

Intervention: Between October 2014 and December 2014, three CSOs trained and engaged 140 community Health Volunteers (CHVs.) in Kakamega, Kisumu and Machakos. CHVs. visited household of notified bacteriologically confirmed TB cases and emphasized on drug adherence, and health education on TB (and MDR TB) transmission, diagnosis, management and prevention, stigma and discrimination, HIV testing and nutrition

management. TIBU data for the three counties was extracted and treatment outcomes analysed.

Contacts were screened and identified presumptive TB clients referred to diagnostic facilities. CHVs. were reimbursed transport per household.

Results: Of the 940 pulmonary bacteriologically confirmed patients, 386 were visited. 1,740 contacts were given health education and screened, 177 presumptive clients were referred and 14 (8%) diagnosed with TB. Evaluated treatment outcomes for 386 patients were: cured (73%), Treatment complete (17%) (90% treatment success rate), died (4%) (Which 3% were TB-HIV co-infected), lost to follow up (3%), transfer out (2%) and failure (1%). This contributed to treatment success rate of 86.4% in the three counties.

Lessons learnt: CSOs through CHVs. plays a role in contributing to treatment success rate of the pulmonary bacteriologically confirmed TB cases.

Conclusion and Recommendation: Health education at the household level for all the TB patients undergoing treatment and the family members is key in increasing treatment success rates and identification of the missing TB cases.

PD-810-28 Evaluation of the knowledge of registered nurses about TB and MDR-TB in Lesotho

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Background: TB and HIV co-infection are major cause of morbidity and mortality in Lesotho. The Lesotho Nurses Association (LNA) is a professional Association which runs a Wellness Centre for health care workers for complete health care services including HIV care for health care workers and their families in Lesotho. Data was collected to assess the knowledge of Nurses who were trained of TB and TB-MDR for four days

Methods: LNA Wellness Centre conducted a training of TB for 32 Nurses with the aid of the International Council of Nurses (ICN) in February 2016. The knowledge for the participants was measured at the beginning of the training and at the end through use of pre and post test questionnaires. The areas addressed were knowledge of nurses towards mode of transmission, TB infection control, MDR-TB management, and feeling comfortable around TB patients.

Results: 29 (91%) of Nurses reported comfort working with TB patients following the training compared to 25 (78%) during the pre-test. 24 (75%), understood the risk factors associated with TB as compared to only 4 (13%) who had knowledge before. The mean answers increased from 64% on the pre-test to 89% on the post-test and 66% thought TB infection and TB disease are the same while during the post test, 97% said they are not the same. 100% correctly responded that TB is caused by bacteria while during pretest 97% got the answer correct. After the training, 97% understood that TB is

a major cause of morbidity and mortality in children compared to before when 72% knew the correct answer. **Conclusions:** It was identified that the knowledge for the Nurses improved after the TB training and that there is still stigma associated with TB, which gets better when the correct training is done. LNA Wellness Centre found it appropriate to continue training nurses on TB and MDR-TB along with supporting them with new information as it comes for them to be comfortable around TB patients. Supportive visits to help nurses disseminate the information to their colleagues and allied Health professionals within six months after the training was found necessary.

PD-811-28 Finding TB in India via active pharmacy engagement: early results from the IC-IMPACTS Study

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Background: India accounts for one-third of the 'missing 3 million TB cases' and diagnostic delays, averaging 2 months, contribute to high morbidity and mortality, and transmission. Pharmacies are the first point of contact for 25% of undiagnosed patients, yet few studies have successfully engaged them in active TB screening services to help shorten the diagnostic pathway.

Methods: The IC-IMPACTS Study engages 105 community pharmacists in Patna, Bihar, in a novel TB screening and referral service to improve early TB case detection, in collaboration with World Health Partners (WHP), via 1) pharmacist education and training; 2) e-referral of adult TB symptomatic patients (cough >2 weeks) for a chest radiograph (CXR) and/or doctor consultation; and 3) pharmacist incentives (Rs. 100 per referral) and e-health messaging. Patient test and treatment costs are covered by WHP's existing private provider interface agency program. Pharmacies are recruited under a step-wedge design (Stages 1-3) in three city blocs. The intervention is being evaluated using quantitative and qualitative methods.

Results: We report findings from the first 3 months of implementation at 60 pharmacies (Stage 1-2). Of 325 CXR referrals made, 271 (83%) were completed, and 144 (53%) were found to be abnormal. Of 152 doctor referrals made, 146 (96%) were completed, 60 (41%) were referred for a sputum and/or GeneXpert test, and 45 TB cases were notified, all of which initiated treatment. Seven (15%) TB patients had microbiological confirmation. The median duration of TB symptoms among notified patients was 30 days (IQ 21-90), and median time from pharmacy contact to treatment initiation was 6 days (IQ 2-14). In pharmacist focus groups, the intervention was found to be highly acceptable, and improved their credibility and trust in the community. Challenges identified include consumer demand for over-the-counter medicines, patient loss to

follow-up after CXR referral, and high pharmacist workload.

Conclusion: Preliminary results from the IC-IMPACTS Study are promising. Lessons learned have been applied to tailor Stage 3 in an integrated knowledge-transfer approach to implementation. The study may serve as an effective pilot for broader expansion in similar high-burden communities, where novel initiatives are urgently needed to 'find' undiagnosed TB.

PD-812-28 Capacity building of primary care providers to improve TB case detection in Georgia

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Background and challenges to implementation: Engagement of primary care providers (PCP) is a critical strategy for improving detection and care of tuberculosis (TB). In Georgia, there is a need for greater involvement of family physicians and nurses in TB management. More than 90% of Georgian citizens can access PCPs within 20 to 30 minutes. While TB specialists are only available at district levels, thus are not easily reachable for rural and remote dwellers. Strengthening capacity of PCPs in TB detection and care is a significant step towards improving access to and quality of TB services.

Intervention or response: In 2011-2015, the USAID TB Prevention Project implemented various educational interventions to build capacity of front-line providers in TB control. The project covered 90% of rural family physicians and nurses countrywide with 2-day training course in TB management. Real case scenarios were compiled into the case discussion bulletins issued quarterly. First ever in Georgia, the 90 minutes online training course was developed to encourage self-study by private providers. Classroom based knowledge oriented sessions were complemented by on-site performance appraisal visits to observe changes in TB management practices and provide mentoring to fill identified gaps.

Results and lessons learnt: Training resulted in improving PCPs' ability for recognizing TB signs and symptoms. The proportion of TB suspects referred by trained family physicians to TB service sites for diagnosis has increased from 2% in 2012 to 18% in 2015. One of the important outputs of this training was adjusting time and place for providing DOT considering patients' needs and expectations. Performance appraisal revealed positive changes in providers' communication skills including TB counseling. Moreover, it proved that interactive and solution-oriented learning improves providers' performance by promoting positive attitudes, encouraging creative problem solving and building self-confidence and responsibility.

Conclusions and key recommendations: Capacity of PCPs in TB management can effectively be built through various learning initiatives. Results can be maximized if traditional training sessions are coupled with modern

approaches such as real case discussions and availability of online resources created in the local language. PCPs should have unlimited access to internet to keep their knowledge up -to-date.

PD-813-28 Social and behavior change initiatives to improve TB detection and treatment adherence in Georgia

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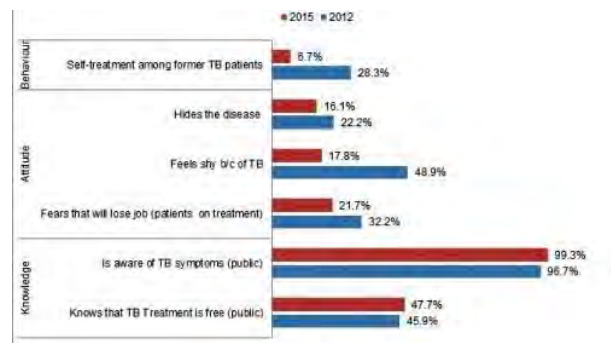
Background and challenges to implementation: Georgia faces significant challenges in controlling TB epidemic. The high level of TB related stigma, low awareness of the importance of good treatment adherence, lack of transportation means for attending DOT sessions complimented with limitations in quality of care result in the high loss to follow up rate (32% in 2013 MDR-TB Cohort) and a growing proportion of MDR-TB cases.

Intervention or response: USAID Georgia TB Prevention Project has been supporting implementation of population based social and behavior change communication (SBCC) campaigns aimed at improving health seeking and TB treatment adherence behaviors since 2012. The campaign was informed by the Knowledge, Attitude and Practices survey conducted at a startup. The groups targeted with educational interventions included current and former TB patients, students, schoolteachers, and front line health care providers. The project used popular TV channels and specifically designed printed materials on TB symptoms and available diagnostic and treatment services. Health care providers received training followed by on-site performance review and mentoring to enhance positive changes in TB detection practice.

Results and lessons learnt: As revealed by two consecutive KAP surveys in 2012 and 2015, interventions led in statistically significant improvement in TB related knowledge and reduction in stigma among TB patients, public and health care providers. These changes stimulated positive health seeking behavior among patients and improved referral practice. The proportion of TB presumptive cases referred by PHC providers to TB specialists increased from 2% in 2012 to 18% in 2015. Number of individuals tested on TB has increased by 18% since 2012. The self-treatment rate has significantly decreased: only 6.6% of study participants reported self-treatment compared to 28.3% from previous study in 2012. Disappointingly, the SBCC interventions did not improve adherence behavior.

Conclusions and key recommendations: SBCC activities have good potential to improve TB related knowledge, attitude and stimulate behavior change among general public, health care workers and TB patients. However, improving knowledge and developing positive attitudes alone cannot lead to significant behavior changes unless there are other motivators and enablers in place for both health care providers and patients.

Figure Changes in TB related knowledge, attitude and behavior



21. Adult lung health in Africa and Asia

PD-814-28 Correlation between body mass index and forced expiratory volume in one second (FEV₁% predicted) in patients with COPD

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Background: Reduced physical performance in Chronic Obstructive Pulmonary Disease (COPD) patients is a result of several associated conditions such as loss of fat free mass, muscle dysfunction, osteoporosis, depression and increased systemic inflammation. Spirometry is used for confirming the diagnosis as well as grading the severity of COPD. It is well documented that low FEV₁ is not the sole factor linked to increased morbidity and mortality in COPD. In our clinic we observed that leaner patients suspected of having COPD showed poorer spirometry results. We did this study with an intention to see if any relationship truly exists between BMI and the spirometric parameter namely, post bronchodilator FEV₁% predicted in COPD patients.

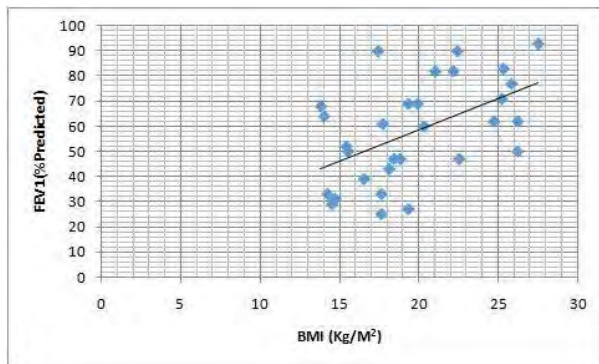
Methods: This was a hospital based cross-sectional study conducted over a period of 3 months. After fulfilling the inclusion and exclusion criteria, spirometry was performed in 43 patients, both males and females suspected of having COPD. Thirty patients had both clinical and spirometry findings required for the diagnosis. The data was analysed using Spearman's correlation coefficient with the help of SPSS software.

Results: Spearman's correlation coefficient (r) between BMI and FEV₁ (% predicted) was determined using SPSS version 21 and was calculated to be 0.49 with a P of 0.006 showing a statistically significant correlation between the two variables.

Conclusions: In our study, body mass index and FEV₁ (% predicted) showed a statistically significant correlation. Patients with low BMI had more severe airflow

limitation. This low BMI could be a consequence of COPD. High energy expenditure and low energy intake may be causing nutritional depletion in COPD patients. These observations have led to a number of trials to intervene with nutritional support for patients with COPD. Low BMI is one of the independent predictors for mortality in patients with COPD. These results support the use of BMI as an important variable to grade COPD.

Figure Scatter diagram



PD-815-28 Community-based screening for chronic obstructive pulmonary disease among the elderly in an urban area of South India

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Background: Underdiagnoses of chronic obstructive pulmonary disease (COPD) is common as this disease is often not recognised and diagnosed until it is moderately advanced. This study was an attempt to find the burden of COPD among elderly urban population.

Material and methods: This community based observational study was conducted among 1037 elderly people in urban areas of Puducherry in India. Participants were recruited using multistage random sampling technique. IPAG questionnaire [cut off score - 17 (positive predictive value: 92%)] was administered among all study subjects. We compared quantitative parameters between COPD and non-COPD subjects using the student *t*-test and χ^2 test was applied for qualitative variables.

Results: Among 1037 subjects, 435 (41.9%) were male and the proportion of smokers among them was 16.5%. A positive IPAG questionnaire for COPD (≥ 17 points) was obtained in 342 (33.1%) subjects. Based on the responses by the probable COPD subjects, 69 (22.2%) had no cough, 215 (62.9%) reported sputum production in the absence of a cold, 186 (54.4%) cough up phlegm (sputum) in the morning, 162 (47.4%) had frequent or occasional wheezing and 113 (33 %) reported to have or had any allergies. Age and body weight found to be associated with positive IPAG questionnaire. Probable COPD was significantly higher among smokers (52.9%) as compared to non-smokers (31.7%) ($P < 0.01$).

Conclusions: Proportion of subjects with possible COPD was high in community. IPAG questionnaire was an easy to administered tool for screening of COPD and little expertise is sufficient for its administration.

PD-816-28 Prescription practices rationalized by the Practical Approach to Lung health in Kerala, India

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Background and challenges to implementation: In India, protocols are available for management of patients with chronic respiratory illnesses in academic circles and tertiary care centres. However, no definite protocol for their diagnosis and management is practiced at primary care level, except for Tuberculosis. Practical Approach to Lung Health (PAL) is a patient-centred approach to improve quality of diagnosis and treatment of respiratory diseases in primary care setting. Kerala, the Indian state piloted PAL from May to November 2015.

Intervention or response: Sixteen institutions providing primary care services in three health blocks in the district of Kollam were selected for piloting PAL. These areas were selected to represent the state geography and health care delivery. Institutions included 12 Primary Health Centres and 4 Community Health Centres with a daily OPD attendance ranging from 70 to 200 in PHCs and 120-400 in CHCs. Clinical care team included a doctor, staff nurse and pharmacists and the field care team included multipurpose health workers. Health staff were trained using technical and operational guidelines developed for PAL. Patient-wise register of chronic respiratory diseases (CRD), an OPD register and a drug stock register were maintained in all institutions.

Results and lessons learnt: In PAL institutions, mean number of drugs prescribed for CRDs was 3.88 (SD 1.50) and 2.73 (SD 1.18) at baseline and after six months respectively ($P < 0.001$). Adjusted OR for prescribing an injection to a CRD patient in PAL institutions was 0.39 (95%CI 0.20-0.74, P 0.004) and for antibiotics was 0.34 (95%CI 0.15-0.75, P 0.008) compared to baseline. Use of injectable Theophyllin, dexamethasone, Ciprofloxacin, Amoxicillin and Amoxicillin Clavulanic acid combination declined by 48.19%, 30.82%, 46.02%, 17.99% and 24.62% respectively.

Conclusions and key recommendations: Adherence to PAL guidelines rationalized the prescriptions in primary health care setting in India. Rationalization caused large reduction in consumption of antibiotics and other drugs. Decrease in prescription of drugs used to treat MDR-TB and XDR-TB (quinolones and amoxicillin-clavulanic acid) was notable. Since PAL deploys bronchodilators and steroids through inhalational route, number of injections reduced drastically.

PD-817-28 Delivering integrated chronic lung health care at primary health care level: a process evaluation

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Background: There is generally no systematic care for COPD and asthma in primary care facilities in Pakistan. We developed a set of implementation products, based on international guidelines, for delivering integrated asthma/COPD care at primary health care facilities in Pakistan. To generate evidence for potential future scale-up, we are assessing the effectiveness of the intervention through a health facility (cluster) randomized controlled trial. We are conducting a process evaluation to assess fidelity to the intervention, assess the feasibility and inform modifications, if any, in the intervention details.

Methods: The whole care process was split into six sets of care tasks which are: clinical assessment and diagnosis, drug prescription, patient counseling, record keeping, follow-up adherence, and referral. The experience of each care-task (i.e., about the what? how? why?) was reviewed through applying three mutually complementing methods: a) patient records have been reviewed for these facility practices and analysed using SPSS (version-20), for the care data on 445 asthma and 322 COPD registered patients; b) semi-structured interviews by social researchers with 10 care providers/ managers and 16 patients to understand the 'how' and 'why' of the on-ground care practices; c) onsite observation of the care setting at four Rural Health Centres facilities. The data on each set of care-tasks, from these three complementary sources, will be compiled for a set of findings about the feasibility and inform modifications, if any, in the intervention details.

Results: Preliminary review of incomplete data indicates various care-quality challenges in each of the six sets of asthma/COPD care tasks. These findings will be further elaborated once the complete set of care and qualitative explanatory data is made available by mid-2016.

Conclusions: The Directorate General of Health Services, and WHO as a technical partner in this whole exercise, will guide the future uptake of the study results for province wide scaling of integrated asthma/COPD care intervention. Beyond the Punjab Pakistan, the experience will inform on using process-evaluation alongside trials and other evaluations of contextualized country programme interventions.

PD-818-28 A development study of pulmonary rehabilitation for patients with chronic lung disease in Uganda

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Background: Chronic lung disease (CLD) is a growing burden in Uganda. There is no useful treatment, but sufferers have poor health status and often are stigmatised. We aimed to test feasibility of a pulmonary rehabilitation (PR) programme in Kampala, Uganda, and adapted traditional PR for patients with post-TB lung disease and COPD.

Methods: In a development study, respiratory specialists, nurses and physiotherapists formed a PR team. The exercise regime was based on conventional PR; the education programme covered normal lungs, post-TB damage and COPD including breathlessness, exercise, nutrition, smoking and drug treatments. Qualitative and quantitative assessment of the programme included recruitment, retention and outcome measures including exercise capacity and health status questionnaires.

Results: In March 2015-December 2015, 4 groups were conducted. In total we screened 193 (post-TB 113 and 80 COPD) patients, 72 were assessed 46 were suitable and 44 started rehab (17 male; mean age 44 years, range 17-83) with 42 (95%) completing and 39 followed 6 week after. Main outcomes in Table 1.

Conclusions: PR is feasible and appears effective in CLD and post TB patients in Uganda, but an adequately powered controlled trial is needed to confirm this. Rehabilitation offers a new and sustainable therapy for the neglected problem of chronic lung disease in low to middle income countries. This study provides patient and stakeholder feedback to inform design and implementation of a full trial planned for Zambia, Kenya and Tanzania.

Table PR outcomes

	Start	End	6 weeks after
Incremental shuttle walk test	298	380	374
Clinical COPD questionnaire	1.8	0.97	0.84
Sit to stand test	10.6	7.9	7.4

PD-819-28 Prognostic factors for interstitial lung disease with microscopic polyangiitis

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Background/purpose: Many patients with interstitial lung disease (ILD) complicated by microscopic polyangiitis (MPA) show a UIP pattern on chest CT. The prognosis is poorer than that of ILD-free MPA(1). To investigate the prognosis of pulmonary fibrosis with microscopic polyangiitis (MPA-ILD) and prognostic factors.

Methods: Of patients with MPA who were admitted to our hospital between 2011 and 2014 based on the EMEA classification in 2010, the subjects were MPO-ANCA-positive patients with ILD on HRCT. Using the clinical data and fibrosis score on HRCT(2), we examined prognostic factors.

Results: There were 42 patients with MPA-ILD, consisting of 20 males and 22 females, with a median age (interquartile range) of 73 years (range: 69-76 years). The MPO-ANCA, KL-6, Aa-DO₂, %FVC, %DLco/VA, and RV/TLC values at the start of treatment were 189 (52-459) EU, 446 (261-615) U/mL, 25.4 (12-34), 81.3 (69-95)%, 61.4 (45-71)%, and 41.1 (33-50)%, respectively. Concerning HRCT images, 30 patients showed a UIP pattern, and 12 showed a non-UIP pattern. PSL was administered to 41 patients. In 37, it was combined with immunosuppressive drugs (CY was used in 16). In 8, apheresis was performed. In 37 patients, the MPO-ANCA level was maintained below the detection limit. With respect to the prognosis, 8 patients died (exacerbation of interstitial pneumonia: 2, infection and alveolar hemorrhage: 2, pulmonary hypertension: 1, sudden death: 2, and renal failure: 1). The 5- and 10-year survival rates after the start of treatment were 81.6 and 68.0%, respectively. Univariate analysis using Cox's proportional hazard model showed that prognostic factors for lung disease-associated death included the HRCT score ($P < 0.001$), CPFE ($P = 0.025$), and administration of CY ($P = 0.041$). However, on multivariate analysis of these factors, the HRCT score was significantly correlated ($P = 0.006$).

Conclusion: Treatment for MPA-ILD was continued, and the prognosis was more favorable than previously reported. Marked fibrosis and CPFE at the start of treatment were considered to be prognostic factors for lung disease-associated death. Immunosuppressive therapy early after onset may improve the prognosis of MPA-ILD.

PD-820-28 Smoking and lung cancer risk in Sri Lankan men: a case-control study

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Background: Although tobacco smoking is identified as a major risk factor for lung cancer in the world, no studies have been conducted in Sri Lanka to measure the level of risk of lung cancer among smokers. The study was done to assess smoking as a risk factor for lung cancer and to assess the adjusted Odds Ratio (OR) of smoking for lung cancer among adult males in Sri Lanka.

Methods: A case control study was done among 62 newly diagnosed male lung cancer patients presented to National Cancer Institute- Sri Lanka. Four controls per case were randomly selected from the same geographically defined area matched for the age of the cases. Controls who were medically examined to confirm as not

having lung cancer and selected by a household survey. Information on smoking, other potential risk factors and confounders were obtained using an interviewer-administered questionnaire.

Results: All 62 cases and 246 out of 248 controls participated in the study. When the effects of confounding variables were controlled, ever smokers were found to be at 10.74 times (3.54-32.59) higher risk of lung cancer compared to never smokers. Other significant risk factors for lung cancer among the males, after being adjusted for the confounding were having a low educational level (a highest of passing Grade 11) (OR 5.61, 2.37-13.28), having been ever exposed to X-ray (OR 2.81, 1.14-6.94) and having a family history of any cancer (OR 2.83, 1.09-7.30). Being a current alcohol drinker (OR 0.20, 0.08-0.48) was found to be a protective factor. Being the overall prevalence of ever smokers as determined by the community prevalence survey as 54.1% (95%CI 51.1%- 57.0%), Population Attributable Risk Percentage of smoking for lung cancer was 84.04%.

Conclusion: Among adult males in Colombo District, ever smokers have a 10.7 times higher risk of developing lung cancer compared to never smokers and if smoking among males were prevented, 84% of lung cancers cases could be prevented. The risk is far higher than developed countries. These findings needed to be shared among the policy makers and public to implement successful smoking preventive measures.

PD-821-28 Trigger factors for asthma symptoms in Sudan and their validation using skin prick tests

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Background: Asthma morbidity is increasing globally including in low income countries. Many trigger factors for allergic asthma in Sudan have not yet been identified.

Objectives: To determine the trigger factors for asthma symptoms in different regions of Sudan and validating the reported factors using skin prick tests.

Methods: A cross-sectional study was performed in western, northern, eastern and central Sudan during 2009-2010. An epidemiological questionnaire was distributed to university students, academic staff, employee and workers chosen randomly. The questionnaire included cardinal asthma symptoms and their known and local trigger factors. Skin prick tests using quality assured commercial allergen extracts manufactured by NELCO Laboratories, USA, were performed to all subjects reported asthma symptoms. Allergen extracts tested include: House dust, *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, Cat hair, Dog epithelium,

Goat epithelium, Grass pollens, mixed molds, Cockroach, Mosquito, and Mixed feathers.

Results: A total of 3974 respondents (1807 males and 2167 females), aged ≥ 18 were included. Dust and trees were the most prevalent trigger factors for allergic asthma reported by asthmatic subjects in all parts of Sudan. Smoke was most important in eastern Sudan; bat droppings in the west; Lemetti insects in the north; carpet and air-conditioning in central Sudan. Validated trigger factors using skin prick tests showed markedly low results compared to the questionnaire response.

Conclusion: Both indoor (house dust) and outdoor (trees) are important trigger factors for allergic asthma in Sudan. Using indigenous allergen extracts for skin testing will yield better results for validation of the regional allergic status.

PD-822-28 Prevalence of pulmonary involvement in rheumatoid arthritis patients in an Indian population

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Background: Rheumatoid arthritis (RA) is the most common chronic connective tissue disorder that significantly affects lung. The main aim was to evaluate the pulmonary involvement in RA patients and its correlation with duration of RA.

Methods: A total of 100 diagnosed cases of RA, divided into two groups of 50 patients each on the basis of duration of RA: <5 years and >5 years were evaluated. All the patients were assessed for clinical characteristics, High resolution computed tomography (HRCT) thorax, and spirometry findings. Disease severity was assessed by the DAS28 score.

Results: Respiratory symptoms were present in 41% patients. Pulmonary involvement (either abnormal HRCT thorax) in 59.3% patients. Chest X-rays were abnormal in 22% patients. Most common radiological findings on HRCT thorax were interstitial lung disease suggestive findings (31%) and bronchiectasis (21.4%). On spirometry, restrictive defects were found in 33%, obstructive defect in 12% and mixed defect in 6%. FEF 25-75% was abnormal in 18% patients. Risk factors for the presence of pulmonary involvement were increasing age and presence of rheumatoid factor; no association was found with gender, duration of disease, or severity of disease.

Conclusions: The prevalence of pulmonary involvement was found in RA independent of duration of illness, HRCT appeared to be more sensitive tool.

PD-823-28 Computed tomographic pulmonary angiography findings in pulmonary embolism: a report of 38 cases

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Background: Computed tomographic pulmonary angiography (CTPA) is currently the gold standard in the diagnosis of pulmonary embolism (PE). This imaging test is increasingly used in Kinshasa to confirm the diagnosis of PE. This study aim to describe the CTPA findings of 38 cases of PE in Kinshasa hospitals.

Methods: A descriptive study on CTPA findings collected in medical records of 38 cases of PE hospitalized in six hospitals of Kinshasa between 1 January 2011 and 30 April 2014.

Results: The male gender was predominant with a sex ratio of 1.2. The average age of patients was 54.8 ± 14.8 years. Proximal pulmonary arterial clots were found in 47.4% of patients. Both proximal and distal clots were detected in 47.4%. Distal branches were rarely obstructed alone (5.3%). The right pulmonary artery was the most affected (60.5%), followed by the left pulmonary artery (47.5%) and the left lower lobe pulmonary artery (47.1%). The most common isolated indirect signs were pulmonary infarction (22.5%) and pleural effusion (12.5%). The following associations: pleural effusion-pulmonary infarction; pleural effusion-atelectasis; pleural effusion-atelectasis-pulmonary infarction were respectively found in 7.5%, 5.0% and 2.5% of patients. There were not indirect signs in half of cases.

Conclusions: Direct signs of PE were dominated by obstruction of the pulmonary arteries and their proximal branches. Indirect signs were represented by pulmonary infarction followed by pleural effusion.

22. Childhood TB clinical and outcomes

PD-824-28 Two's company, three's a crowd: tuberculosis in HIV-infected South African children with complicated severe acute malnutrition

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Background: The combination of severe acute malnutrition (SAM) and HIV poses a unique clinical challenge and is associated with high mortality in children in resource-limited settings. TB is commonly seen in association with either of these conditions, but the

spectrum of TB in a cohort of children with both SAM and HIV has not yet been described.

Methods: We report the rates of clinically-diagnosed and microbiologically-confirmed TB in children enrolled in a prospective study carried out in an urban South African setting, the inclusion criteria for which were SAM (diagnosed according to WHO criteria) and newly-diagnosed HIV infection.

Results: 82 children (46.3% female, mean age 23 months) were enrolled in the study. The incidence of TB was 25.6%. Eight children had microbiologically confirmed pulmonary TB while 13 were clinically diagnosed: five whose treatment was commenced in another setting before transfer to our centre (two suspected pulmonary, two suspected multiorgan and one suspected abdominal TB), and eight who were commenced on treatment in our centre but never had TB isolated from a clinical specimen (one meningitis and seven pulmonary). The Xpert-MTB/RIF platform—introduced to our centre mid-way through the study—was employed in 45 patients and was positive in two, but these were also smear- and culture-positive. The ratio of confirmed vs. empirically-treated cases did not change following the introduction of Xpert (5:7 pre, 3:6 post, $P = 0.199$). Univariate analysis did not reveal any clinical or biochemical parameters at admission that were predictive of a subsequent diagnosis of TB. Mortality in children treated for TB was 19% at 6 months, compared to 13% in the remainder ($P = 0.49$).

Conclusions: TB is common in children with SAM and HIV. This study highlights the importance of TB in this highly-vulnerable population and underlines the need for better diagnostic strategies in paediatric TB.

PD-825-28 Integrating routine TB screening for children in malnutrition programmes: a review of country guidelines from high TB burden countries

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Background: Childhood tuberculosis (TB), HIV and malnutrition are major public health challenges contributing to significant child morbidity and mortality. The World Health Organization estimated 1 000 000 cases, and 136 000 deaths due to TB in children aged <15 years in 2014. The majority of childhood TB cases remain undiagnosed, partly due to a lack of capacity, but also a lack of awareness both by TB as well as maternal and child health, nutrition, and other providers who often serve as the first point of care for children affected by TB. Malnutrition is a co-factor in approximately 45% of deaths in children <5 years. TB and malnutrition are closely linked; malnutrition increases the risk of TB and TB can cause or worsen malnutrition. Studies have found TB prevalence as high as 24% among children with acute malnutrition. The WHO 2013 guideline for severe acute

malnutrition recommends TB screening only in the context of HIV. We reviewed guidelines for the management of acute malnutrition from high TB burden countries on whether and how TB and HIV are addressed.

Methods: Guidelines were obtained from the Community-based Management of Acute Malnutrition (CMAM) Forum website as well as country contacts. Information was collected regarding TB symptom screening, TB contact screening, HIV screening, and TB and HIV treatment.

Results: Guidelines from 14 countries were included in the analysis; 10 (71%) identified TB as a potential cause for failure to respond to treatment for acute malnutrition, but only 6 (43%) recommended routine TB symptom screening and 4 (29%) specifically obtaining information about TB contacts. Four (29%) countries recommended treating TB as per national TB programme guidelines in nutrition services. Six (43%) countries recommended or required counseling and testing for HIV in the setting of acute malnutrition. Treatment recommendations for HIV varied with regard to timing and referral.

Conclusions: TB screening is not included in malnutrition guidelines in many high TB burden countries. Routine TB risk assessment, especially of a TB contact, among acutely malnourished children combined with improved linkages with TB services would help to increase TB case finding and impact outcomes for children with TB as well as malnutrition.

PD-826-28 TB case finding among malnourished school-age children

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Background and challenges to implementation: Malnutrition is a known risk factor for developing tuberculosis. Underweight individuals (BMI < 9.5) are up to 3.5 times at risk for TB. Weight loss is also a common TB symptom in children, but diagnosis is difficult because strict symptom criteria have lower sensitivity and specificity in severely malnourished children. The Philippine Department of Education implements a nationwide school-based feeding program in public schools to rehabilitate severely wasted Kindergarten to Year 6 pupils, but this does not integrate TB screening.

Interventions or response: TB screening using TB exposure and symptoms as bases was conducted among severely wasted children in two public schools. Tuberculin skin testing (TST) and chest X-ray were administered in all children regardless of symptoms. Xpert MTB/RIF was recommended for symptomatic children who can expectorate. Based on the National Tuberculosis Control Program, TB was clinically diagnosed when at

least 3 of 5 criteria were met: 1) exposure to a known TB case, 2) symptom criteria for TB (any 3 of 6), 3) positive TST (at least 5mm), 4) chest X-ray suggestive of TB, and 5) any other diagnostic tests suggestive of TB.

Results and lessons learnt: Of 300 eligible severely malnourished children, 246 consented to screening. Twenty-two children were classified as presumptive TB cases based on symptom criteria; none were able to expectorate and submit sputum for Xpert MTB/RIF. Only one of the 22 children fulfilled the clinical criteria for TB. Using exposure, TST, and chest X-ray, four of the children who failed the symptom criteria fulfilled the clinical criteria for TB. This gave a total of five children (2%) diagnosed as TB, a rate much higher than estimated prevalence of TB in the community, which is 0.4% or 417/100 000 (WHO, 2015).

Conclusion: Symptom screening alone may detect only 20% of TB cases among malnourished schoolchildren as most diagnosed TB cases did not fulfill the symptom criteria. Using TST and chest X-ray together with symptom screening increases TB case yield. Screening 50 cases will detect 1 (2%) TB case among malnourished children, which is comparable with household contact screening (CATCH-TB, 2013).

PD-827-28 Tuberculosis pericardial effusions in children

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Background: Although pericardial effusion is a rare manifestation of extrapulmonary TB (EPTB), it is the most frequent cause of pericardial effusion in high tuberculosis (TB) burden settings. There are few reports on TB pericardial effusion in children. We describe the clinical presentation, diagnosis, management and outcome of children with TB pericardial effusion.

Methods: We conducted a retrospective study of all children aged < 3 years diagnosed with bacteriologically confirmed or probable TB pericardial effusion at Tygerberg (TBH) and Brooklyn Chest (BCH) hospitals, Cape Town, South Africa, from January 2011 to December 2015. Children were identified from 3 sources: i) ICD10 hospital discharge codes, ii) an ongoing clinical database of all culture-confirmed TB in children from TBH and iii) clinical notes of BCH admissions (a TB hospital). TB pericardial effusion was confirmed if a pericardial effusion was diagnosed by echocardiography, ultrasound (US) or chest computed tomography (CT), together with bacteriological confirmation of TB (any site). Probable TB pericardial effusion was diagnosed through imaging and clinical presentation compatible with TB pericardial effusion, without bacteriological confirmation.

Results: Thirty-one children (median age 48 months; 19 (61%) male; 10 (32%) HIV-infected) were identified.

The predominant presenting symptoms were weight loss (26; 84%), cough >2 weeks (20; 65%) and fever (14; 45%); predominant clinical signs were hepatomegaly (21; 68%) and peripheral lymphadenopathy (14; 45%). Pericardial effusion was suspected in 19/30 (63%) on chest radiography (CXR), and diagnosed by echocardiography/US in 30 (97%) and on CT in 1 (3%); 8 (26%) effusions were large, 7 (23%) moderate, 13 (42%) small and 3 (9%) unclassified. Anti-tuberculosis treatment was started in all; 14 (45%) children also received prednisone for their pericardial effusion and 3 (10%) received cardiac failure therapy. Five (16%) cases had therapeutic pericardiocentesis. Complications included cardiac tamponade (3; 10%), constrictive pericarditis (3; 10%), of which 2 needed pericardiectomy, and death (1; 3%).

Conclusions: TB pericardial effusions missed by CXR, are detectable on echocardiography / ultrasonography. A high index of suspicion is needed to diagnose this condition which carries a high risk of complications in children and may require specialised treatment.

PD-828-28 Atypical radiological patterns in children with bacteriologically confirmed pulmonary tuberculosis

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Background: Given the paucibacillary nature of disease and sampling challenges, diagnosing pulmonary tuberculosis (PTB) in young children relies on symptom evaluation, contact history and chest radiography (CXR). CXR images considered 'typical' of TB are assumed to result from the Ghon complex and its complications. We interpreted CXRs in children with bacteriologically confirmed PTB and describe images inconsistent with 'typical' patterns.

Methods: Children aged 0-14 years enrolled in a hospital-based diagnostic study in Cape Town, South Africa, with clinical suspicion of PTB and who had bacteriological confirmation on culture and/or Xpert MTB/RIF (Xpert) were included. CXRs (antero-posterior and lateral) were read independently by 2 experts using a standard reporting form, and classified by radiological pattern: 'typical' or 'atypical' of PTB. 'Atypical' CXRs were defined as absence of any of the following radiological patterns - lymph node disease, Ghon focus/complex, expansile pneumonia, pleural effusion, miliary TB, TB bronchopneumonia and adult-type cavitary disease. Logistic regression was used to determine associations between clinical parameters (demographics, symptom duration, TB exposure, tuberculin skin test-TST-positivity), method of bacteriological confirmation and 'typical' radiological pattern.

Results: 93 eligible children had an acceptable quality CXR. 54/93 (58%) were both culture and Xpert-

positive, 24/93 (26%) were culture-positive and 15/93 (16%) were Xpert-positive. 18/93 (19%) CXRs were classified by 100% inter-reader consensus as being 'atypical' of PTB. 'Atypical' radiological patterns included normal ($n = 4$), lobar pneumonia ($n = 5$), lower respiratory tract infection ($n = 7$), lobar collapse without lymphadenopathy ($n = 1$) and bronchiectasis ($n = 1$). TST positivity ($n = 71$; OR 4.24, 95%CI 1.24-14.51) and bacteriological confirmation by both culture and Xpert ($n = 93$; OR 3.56, 95%CI 1.19-10.55), but not confirmation by either culture or Xpert alone, were associated with a 'typical' CXR. Age, HIV co-infection and nutritional status were not associated with a specific radiological pattern.

Conclusion: The inclusion of only bacteriologically confirmed cases in this cohort of children provides robust evidence that a high proportion of children with PTB present with 'atypical' CXRs. While 'typical' CXR findings support a diagnosis of PTB, 'atypical' findings in the context of high clinical suspicion for disease should not deter clinicians from investigating further with respiratory specimen collection and close follow-up.

PD-829-28 Factors associated with mortality among children diagnosed with tuberculosis in Kampala City, Uganda

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Background: According to the WHO 2014 report, children contribute to over half-a-million new tuberculosis (TB) cases detected, of which 140 000 children died due to tuberculosis that year. The burden is likely to be higher given challenges in childhood TB diagnosis. Achieving the goal of zero TB deaths among children requires an in-depth understanding of the factors associated with these deaths.

Methods: We retrospectively reviewed 486 records of children with TB registered for treatment in 2014, to establish factors associated with their death. We performed a mortality-based analysis by gender, age, HIV status, being on cotrimoxazole or antiretroviral therapy for the TB-HIV co-infected, disease class and type-of health facility.

Results: About half (51%) were males and 244 (46%) were below age five. Classification according to disease category was, 109 (22%) pulmonary-bacteriologically confirmed (P-BC), 272 (56%) pulmonary clinically diagnosed (PCD) and 105 (22%) extra pulmonary (EP). 14

(3%) of the cases were retreatment. 182 (37%) were HIV co-infected. Public health facilities contributed 256 (53%) of the patients. A total of 44 (9%) children died on TB treatment. Death among different categories was 19 (18%) for EP, 6 (14%) for P-BC cases and 19 (7%) for PCD cases. After adjusting for confounding, the odds of death was five times more among EP patients as

compared to the PCD and P-BC combined; four times more among HIV-positive compared to HIV-negative; twice as much for males compared to females, and thrice more among children aged < 5 years (Table). No association was observed between death and the other factors considered.

Conclusion: Extra pulmonary disease, positive HIV status, male sex and age < 5 years were independently associated with death among children on TB treatment in Kampala. We recommend further studies to better understand these and how much they contribute to death to improve management of childhood TB.

Table

Variable	Crude OR	Adjusted OR	CI	P value
EP	3.1	4.5	2.2-9.1	0.00
HIV Positive	2.5	3.6	1.8-7.1	0.00
Male	2.0	2.4	1.2-4.8	0.01
< 5yrs	2.0	2.5	1.2-5.1	0.01

PD-830-28 Factors affecting treatment outcome of childhood tuberculosis in two regions of Ethiopia

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Background: Childhood TB treatment outcome is not routinely evaluated in Ethiopia. It is crucial to understand treatment outcomes for children on anti-TB treatment to devise targeted interventions.

Methods: A retrospective cohort study was conducted among children (under 15 years) on anti-TB drug treatment during 2012-2014. Data were collected from 138 health facilities (98 health centers, 40 hospitals) in Amhara and Oromia Regions. Data on background information, clinical data, laboratory follow-up and final treatment outcome were collected via data extraction sheet from unit TB registers. Frequency and percentage were computed to describe treatment outcomes and backward logistics regression analysis assessed factors associated with successful TB treatment.

Results: A total of 2541 children (below the age of 15) were enrolled on treatment, of which 227 (8.9%) were bacteriologically confirmed, 1218 (47.9%) smear negative pulmonary TB and 1100 (43.2%) extra-pulmonary TB. The TB-HIV co-infection rate was 7.3%. For all forms of TB registered, the treatment success rate (TSR) recorded was 92.2%; 2.8% were deaths and 3.3% transferred out (Figure). Of 227 bacteriologically confirmed TB cases, 74.4% were cured; 18.9% completed treatment. Patient follow-up at health center and HIV-negative status were factors that significantly predicted successful TB treatment: Adjusted Odds Ratio (AOR) [95%CI] of 2.3 [1.5-3.6] and 2.3 [1.3-4.1] respectively (Table).

Conclusion: The large majority of pediatric cases on anti-TB treatment were not bacteriologically confirmed.

Treatment outcomes among the pediatric age group were comparable to the project level TSR of 94%. Decentralized patient follow-up at the health center yielded better outcomes.

Table Factors associated with successful treatment

Variables		TSR (%)	AOR [95%CI]
Health facility	Hospital	86.5%	Reference
	Health Center	94.6%	2.3 [1.5, 3.6]
HIV status	Reactive	88.2%	Reference
	Non-reactive	92.9%	2.3 [1.3, 4.1]

PD-831-28 Excellent outcomes seen in children treated for tuberculosis under programmatic conditions in Cape Town, South Africa

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Background: The public health burden of tuberculosis (TB) in children is significant, constituting approximately 10% (1 million cases, 140 000 deaths) of cases globally. While most high-burden countries have exceeded overall treatment success rates of 85%, South Africa has a success rate <80%. TB treatment outcomes in children are not well documented and risk factors for unfavourable outcomes require investigation.

Methods: A retrospective analysis of children < 15 years of age started on TB treatment in primary health clinics in Cape Town, South Africa, between 2005 and 2012. We investigated demographic and clinical risk factors associated with negative outcomes (death, moved, transferred, loss to follow up, failed or unknown outcome) or death. Generalised estimating equations with logit link were used to estimate the odds associated with negative outcomes. Kaplan Meier survival curves and Cox proportional hazards model were used to investigate mortality.

Results: Of 29 519 children started on TB treatment, 90% were successfully treated and < 1% ($n = 203$) deaths were recorded during treatment. Loss to follow-up was 6% while treatment failure < 0.5%. Overall documentation of HIV status was 55%, but for those treated between 2010 and 2012, >92% had known HIV status. Younger age, being HIV-infected and any extra pulmonary TB were significantly associated with negative treatment outcome. In multivariable Cox regression younger age and HIV remained significant. Children aged 0-2 years had 3.13 times (95%CI 1.777-5.519) increased hazard of death compared to children aged 10-14 years. HIV-infected children had 6.85 times (95%CI 4.60-10.19) increased hazard of death compared to HIV-uninfected children.

Conclusions: We found excellent treatment outcomes in children <15 years of age under routine programmatic conditions with low rates of treatment failure and death.

HIV-infected children and those < 2 years of age were at significantly higher risk of death. These paediatric subgroups require additional focus to mitigate death.

PD-832-28 Risk factors for treatment default in pediatric tuberculosis cases

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Background: Failure to complete treatment remains a major challenge in the management of childhood TB. We sought to identify risk factors for incomplete treatment in pediatric cases admitted to the Pediatric Ward-Pham Ngoc Thach (PNT) hospital in two years 2011-2012.

Methods: We conducted a questionnaire-based, case-control study between August 2014 and May 2015. A total of 185 childhood TB patients were enrolled into the study: 85 cases (patients identified as loss to follow-up or self-discharged) and 100 controls (patients recorded as successfully completing therapy). All analyses were done with R version 3.1.0 (R Foundation for statistical computing, Vienna, Austria). Two-sided $P < 0.05$ were regarded as statistically significant.

Results: All patients were new TB patients, approximately two-thirds of these children (61.2% for cases and 59% for controls) were between 0-4 years old, female accounted from 40% (controls) to 47% (cases), 74% of controls vs. 33% of cases are living in HCMC. Pulmonary TB form accounted from 47% (cases) to 58% (controls). Geographic location or the distance from patient's house to health facilities is a really risk factor for loss-to-follow-up among pediatric TB patients (OR: 17.14; [95%CI 5.76-51.0]; $P < 0.001$) and children who had high education level and high-income parents were less often defaulted compared with children who had low education level and low-income parents (OR=0.42 [95%CI 0.01-0.86], $P = 0.018$ and OR=0.37 [95%CI 0.18-0.79], $P = 0.010$, respectively). Long treatment durations were a risk for default (OR = 2.63 [95%CI 1.14-6.03], $P = 0.022$). Larger households of more than 5 people appeared to be protective with a lower risk of default (OR = 0.18 [95%CI 0.39-0.82], $P = 0.027$). Especially, in our study, 29.4% of loss to follow-up patients died or unrecovered.

Conclusions: Pediatric TB patients who had low education level and low-income parents or who lived in mountain/remote or rural area are particularly at risk for loss to follow-up from TB treatment. Socioeconomic supports targeting the most at-risk groups may help to increase treatment adherence in Viet Nam and similar areas of high pediatric TB burden.

PD-833-28 Investigating loss to follow-up among adolescent TB patients in Gaborone, Botswana

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Background: There is growing evidence that adolescents with tuberculosis (TB) face greater challenges in adhering to and completing treatment than do adults. Preliminary data has raised concern over higher loss to follow-up (LTFU) among adolescents. Here we compare adolescent TB treatment outcomes with those of youth and adults, and investigate the ultimate outcomes of those adolescents who have been lost to follow-up in Gaborone, Botswana.

Methods: This is a retrospective cohort study of adolescents, youth, and adults who were treated for TB in Gaborone from January 2008 to December 2014. Botswana National TB Programme (BNTP) treatment registers from nine high-burden public clinics in Gaborone were reviewed. Every adolescent (10-19) and youth (20-24) registration was sampled. For convenience, a systematic sample of every third adult registration was used. For the analysis, we excluded TB cases that transferred-out or where the outcome was not yet documented in the register. Clinical characteristics were described and treatment outcomes were compared between adolescents, youth, and adults. Among those adolescents LTFU, we sought to determine ultimate outcomes from review of the paper BNTP clinic register, patient cards, the BNTP national electronic TB registry, and the national death registry.

Results: We enrolled 130 adolescent, 234 youth, and 610 adult TB cases. The proportion of LTFU was greater among adolescents, 13/120 (10.8%), compared with 16/210 (7.6%) among youths and 30/548 (5.5%) among adults ($P = 0.031$). Investigation of the 13 adolescent LTFU cases on review of the paper BNTP register revealed that one (7.7%) died and three (23.1%) restarted treatment - of these, one completed treatment, and two were again lost to follow-up. Further investigation into the ultimate outcomes among the LTFU cases is ongoing and will be completed before the Union meeting.

Conclusions: Adolescents are at increased risk for LTFU from TB treatment in Gaborone, Botswana. Further work is needed to determine the ultimate outcomes of those adolescents who are LTFU and to explore the outcomes of adolescent TB patients in different settings. A greater understanding of the multifactorial challenges facing adolescents in TB treatment is needed along with targeted interventions to improve adolescent TB care and outcomes.

23. Childhood TB around the world

PD-834-28 Community-based tracing of contacts to improve tuberculosis screening and uptake of isoniazid preventive therapy among children

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Background and challenges to implementation: Children aged <5 years in contact with tuberculosis infectious patients are at risk of infection and early progression to disease. This can be prevented using Isoniazid Preventive Therapy (IPT). Kenya recommends screening of all child contacts and 6 months of IPT to eligible children below five year. The strategic plan 2015 to 2018 indicates limited screening among child contacts with a small proportion of those eligible receiving IPT. Amref Health Africa Global Fund TB Project through Civil Society Organizations (CSOs) has been working with the community Health Volunteers (CHVs.) to strengthen household contact screening countrywide.

Intervention: Between January to June 2015, 3022 CHVs. visited households of bacteriological confirmed TB patients and screened their contacts for TB. Child contacts were screened and referred to the nearest health facility for further investigations and initiation of IPT for children under five. Follow up was done to ensure clients reached the health facility. CHVs. received an incentive of USD 8.4 per household visited. Data on contact tracing and referrals was analyzed from the project data and number started on IPT analyzed from TIBU a national case based electronic system.

Results and lessons learnt: From the 10 032 households visited, 23 063 contacts were screened out of which 7782 (34%) were children. A total of 2577 (33%) under five years were referred for further diagnosis and IPT of which 689 (27%) were started on IPT and documented in TIBU. CHVs. are scaling up tracing and referral of child contacts. Low uptake of IPT was attributed to barriers to quality diagnostic services for children due to limited access to affordable, X-rays for TB diagnosis. GeneXpert machines were not strategically placed and networked to ensure equitable access to all children. Incomplete documentation of IPT data was experienced.

Conclusions and key recommendations: Household screening of contacts led to more children being referred. However uptake for IPT was low. The Ministry of Health should continue to empower CHVs. to improve early diagnosis and prevention of TB among children. The facilities should be well equipped to improve diagnosis of tuberculosis even at the peripherals.

PD-835-28 Risk factors for complicated TB in children aged under 2 years: an observational study in a low-incidence TB country

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Background: Children aged ≤ 2 year-old are at increased risk of TB complications due to immaturity of the innate immune response. The aim of this study was to identify risk factors for TB complications in this age group in a low-incidence TB country (Catalonia, Spain).

Methods: Multicentric observational retrospective study of TB cases in children ≤ 2 years in Catalonia (2005-2013). Epidemiological and clinical data were collected from medical history. TB complication was defined as any tissue damage generating a long-term functional or anatomical impairment post-TB treatment. Statistical analysis was performed with Stata[®] 13.1 package. Ethical approval was obtained from all participant centers.

Results: Overall 134 (49.3% male, median age [IQR]: 13[8-18] months) patients were included, 1.5% (2/134) lost to follow-up, and 18.9% (25/132) diagnosed with TB complications. Most of them (94.8%) were autochthonous. Known active TB at household was in 54.5% (73/134), BCG vaccination in 2.2% (3/134), completed contact tracing in 70.2% (94/134), familiar index case in 59.0% (79/134), and positive TST in 91.0% (122/134) of cases. Median onset symptom prior to diagnosis was one [IQR 0-2] week. HIV-test was unknown in 22.7% of cases, no HIV-infected children. Chest X-ray was compatible with TB in 65.4% (87/133) of children. Completed TB treatment in 99.2% of cases. Pulmonary TB accounted for 94.0% (126/134) of children, and most common complications were lobar collapse (6/126) and bronchial hyperreactivity (5/126); meningitis TB for 10.4% (14/134), with hydrocephalus (2/14) and mental impairment (3/14) as complications; two spinal TB cases developed vertebral destruction and paraplegia. See the Table for multivariable logistic regression analysis.

Conclusions: TB complications represent 18.9% of total TB diagnoses in children < 2 years old in Catalonia. Associated risk factors are not active TB in household, no contact tracing, tachypnea, irritability or neurological symptoms at the diagnosis. TB meningitis is the clinical form with higher risk for complications.

Table

Variables	TB complications (%)	No TB complications (%)	Multivariable analysis (P value)
No active TB in household (yes)	34.9	65.1	=0.009
Irritability/neurological signs (yes)	46.2/85.7	53.8/14.3	<0.0001
Tachypnea (yes)	33.3	66.7	=0.02
TB meningitis (yes)	78.6	21.4	<0.0001

PD-836-28 Paediatric tuberculosis in Timor-Leste: opportunities for improving recognition, diagnosis and prevention

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Background: Timor-Leste has the highest incidence of TB in Southeast Asia but a relatively low rate of paediatric notifications. Bairo Pite Clinic (BPC) in Dili manages more than a fifth of all TB cases in the country. Improved understanding of TB epidemiology in Timor-Leste will inform quality improvement activities focused on recognition, accurate diagnosis and prevention of TB in children.

Objectives: To describe the epidemiology and diagnostic features of notified paediatric TB cases in a major institution in Dili, Timor-Leste, and to compare to national paediatric TB notification rates.

Method: Prospective collection of demographic, clinical and laboratory data for all patients diagnosed with TB at BPC in Dili between January 2014 and December 2014 inclusive. Comparison is made with national notification data with respect to paediatric notification rates.

Results: In total 4090 TB cases were notified in Timor-Leste. Of these, 426 (10%) were children aged < 15 years. BPC notified 886 cases, of which 111 (13%) were aged < 15 years. Of the paediatric cases diagnosed at BPC, contact with a known TB case was reported in 51% (44/87); 14% (15/109) were identified by screening household contacts of infectious index cases. Evidence of BCG vaccination was noted in 63% (36/57) cases. Malnutrition was identified in 51% 40/78; HIV in 4% (2/51) cases with a documented HIV test. Pulmonary TB was diagnosed in 68% (75/111) BPC cases and 75% (318/426) paediatric cases nationally. Bacteriologically confirmation occurred in 7% (5/75) pulmonary cases at

BPC and 11% (36/318) cases nationally. In districts other than Dili and Baucau, 22% (29/131) paediatric pulmonary TB cases were sputum smear positive.

Conclusion: Paediatric TB is common in high burden settings such as Timor-Leste, but is under-recognised. Microbiological confirmation is challenging, and clinical diagnoses are infrequently made, especially in districts outside of Dili and Baucau. Training in recognition and diagnosis of paediatric TB is needed. Consideration should be given to implementing proven specimen collection techniques and strategic use of PCR to improve diagnostic certainty. Malnutrition is an important risk factor in Timor-Leste; HIV co-infection is rarely encountered. Opportunities for prevention include improved BCG coverage and implementation of household contact tracing.

PD-837-28 Factors associated with non-adherence to anti-tuberculosis treatment among children attending three paediatric TB clinics in Kampala, Uganda

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Background: Non adherence to anti tuberculosis treatment is one of the main causes of treatment failure. This study aimed to determine the level of adherence to anti tuberculosis treatment and factors associated with non adherence to these drugs among children in Kampala Uganda.

Methods: It was a cross sectional study with qualitative data component that was conducted at 3 paediatric TB clinics in Kampala from March 2013 to Feb 2014. Adherence to TB medication was defined as taking >90% of the prescribed drugs in a previous month and was assessed using self report. Data was analyzed using STATA version 12. All variables with $P < 0.2$ were entered into logistic regression model to determine the independent predictors of adherence. Qualitative data was analysed using thematic analysis.

Results: A total of 253 children aged one month to 14 years who were on anti-TB drugs for at least 1 month (4 weeks) were enrolled in the study. The overall level of adherence was: 85.4% (95%CI 81-89.8) at one month (28 days) using self report. There was 85% reduced likelihood of non adherence among caregivers who were always able to get their drugs from health facility compared to those who were not able to get drugs. OR 0.15 (95%CI 0.06- 0.37) $P < 0.001$. There was 11-fold increased risk of non adherence among parents who had no confidence in the prescribed drugs compared to those who had confidence in the prescribed drugs. OR 11.17 (95%CI 3.6-34.2) $P < 0.001$. From qualitative data the factors that caused children to miss their drugs included, inability to get drugs from health facility, drug stock outs, forgetting to give the drugs, seeing the child was much better and had improved.

Conclusions: The level of adherence to anti-tuberculosis treatment among children attending TB Clinics in Mulago Hospital, Nsambya Home care and KCCA health centre was high at 85%. Factors which were independently associated with non adherence to anti-tuberculosis treatment included inability to get drugs from health facilities and caregivers who have no confidence in the TB medication prescribed. Ministry of Health should ensure constant supply of anti-tuberculosis drugs in all health centres.

PD-838-28 Window ventilation is an effective intervention for preventing clusters of tuberculosis in schools

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Background and challenges to implementation: Tuberculosis (TB) is one kind of chronic respiratory infectious disease. In the crowded environment, once source of infection appears, it is likely that a cluster of TB will occur with poor ventilation in dormitories or classrooms. In China, areas of the classroom, library and dormitory are not spacious and ventilation is poor, especially in private schools. In 2010 and 2011, two clusters of TB occurred in two schools in Minhang District. TB patients were in the same dormitory or in the same class. Epidemiological investigation showed the TB students had a history of BCG vaccination with no tuberculosis contact history. Doors and windows were often closed because of air conditioning. And dormitory buildings were old, with poor air convection, which were in no state of management. Above all, two events were closely related with more contact among students, poor ventilation and environment of living and learning.

Intervention or response: By the end of 2011, rules of implementation for TB control in public schools had been formulated by Minhang District health administrative department. According to the documents requirements, public schools formulated the system of window ventilation and assigned the specific persons in charge of daily window ventilation and cleaning work of classes and dormitories. The community doctor trains school health care teachers to carry out the overall work management, and supervises school work regularly to identify problems timely and urges to correct them. Health administrative departments and education departments jointly carry out the supervision, and complete the supervision report to inform.

Results and lessons learnt: Since the implementation of the rules, the annual average number of clusters decreased from 1 to 0.25. The only TB outbreak in these years happened at a private high school, fully covered with glass. In addition, the school ignored the rules of window ventilation. In the end, the event was characterized as a case of tuberculosis outbreak caused by the environmental closed and poor ventilation conditions.

Conclusions and key recommendations: Window ventilation is one of the effective interventions to prevent the

clusters of tuberculosis in school, and it is relatively more economical.

PD-839-28 Implementation of task-shifting for childhood TB in Nigeria: the role of pediatricians

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Background: With an estimated prevalence of 330/100 000 TB cases annually and low case detection rate (15% in 2014); the proportion of childhood TB among all notified cases has plateaued at 5-6% for over a period of five years in Nigeria. With over 43% of the population aged less than 15 years, the case detection for TB among this age group is very low, given the high endemicity of TB in Nigeria. Among other factors attributed to this include, inadequate number and poor distribution of skilled health care workers, poor access to appropriate diagnostic facilities, and general low awareness on childhood TB among health care workers.

Objective: to describe the engaging process and the role of pediatricians in the implementation and rolling out of task-shifting for childhood TB.

Methodology: Stakeholders meeting with Nigerian pediatric infectious diseases, participatory review of training materials, conduct of training of trainers among pediatricians, and development of pediatric desk guide (SOP) for general health care workers. In 12 priority states, five facilities were selected based on availability and utilization of any form of childhood services; pediatricians were assigned facilities for on the job training and monthly mentoring visit, and facilities were linked with NTP for regular supplies of commodities and routine monitoring and evaluation.

Results: A total of 15 pediatricians were engaged in the 12 states, 60 facilities supported, and 450 health care workers trained. Within two-quarters there was an increase in childhood TB case notification across the 12 states, the notification varied by states with a range of 2.6% to 10%. On quarterly basis the proportion of childhood TB among notified cases was 5.5% in quarter 3 and 6% in quarter 4 (1098 childhood TB cases among a total of 19 093 TB cases notified in the 2 quarters). 45% of the childhood TB were less than 5 years and the male/female ratio was 1:1. As an ongoing intervention, the project will continue to monitor the performance of these facilities in case finding and treatment outcome.

Challenges: Low uptake and utilization of GeneXpert and access to X-ray and weak support for two-way referral system.

PD-840-28 Implementation of gastric aspiration rooms for diagnosis of pediatric tuberculosis in two health facilities in Lima, Peru

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Background and challenges to implementation: Gastric aspirates are often used to diagnose TB in children who cannot produce a sputum sample. Although gastric aspirate constitutes standard of care for TB diagnosis in children < 15 years who cannot produce sputum in Peru, many facilities do not conduct this procedure due to competing priorities and limited resources and training. To increase access to gastric aspiration in high TB burden and low-income areas in Lima, Peru, we planned to implement a room in each of five health centers that meet biosafety standards for the procedure and also train nurses in the procedure

Intervention or response: Five health centers that did not have rooms for gastric aspirates were selected but only two have been implemented. Among the TB program of these centers were identified 5/5 nurses without experience in gastric aspiration. An expert nurse in the procedure led the training and determined that nurses in training need to perform at least three procedures to be considered qualified. Training needs about the gastric aspirate were established among the nurses based on their previous knowledge about the procedure. Then, on-hands training was implemented, assessing their skills during the procedure. After training, 4/5 nurses were qualified as best skilled. Skilled nurses participated actively in the implementation of gastric aspirate rooms

Results and lessons learnt: Between May 2015 and January 2016, 2/5 health centers performed 63 gastric aspirates on 43 children; this compares to zero procedures in each health facility prior to intervention implementation. Among the assessed children, two were diagnosed with TB after obtaining positive cultures in their gastric aspirates. Prior to training some nurses were reluctant to consider the training and/or the gastric aspirate procedure due to fear of contagion and/or a lack of understanding of the role of gastric aspirate when diagnosing TB in children. High staff turnover challenged training: two of five nurses were transferred to other health centers without having completed training

Conclusions and key recommendations: Through nurse training and conditioning rooms for gastric aspirates in health centers, we increased access to the procedure, which will likely facilitate TB diagnoses among children

PD-841-28 Management of children with tuberculosis at a referral hospital in Malawi

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Background: Malawi is one of the countries with high TB notification rates. These high notifications are mainly

due to high HIV prevalence at 10% among general population and 54% among TB patients.

Aim: To determine the number of paediatric TB patients who accessed TB-HIV services at Kamuzu Central (referral) Hospital (KCH) in Malawi in a ten-year period (2006-2015).

Intervention: Malawi National TB Programme (NTP) has put in place a recording and reporting system for TB patients, including TB-HIV services data for several years; however, paediatric TB has not been systematically reported to NTP. We therefore determined the number of paediatric TB patients for a ten years period from KCH including TB-HIV services and treatment outcomes for all forms of paediatric TB patients.

Methods: TB patients' records (2006-2015) were reviewed. Existing national data for all patients (children/adults) reported at the national level was used as a control.

Results: TB case notifications among paediatric patients at KCH decreased at an average rate of 6-8% per year from 2006-2015. The decrease was also observed among all other patients (2-5% per year). Paediatric TB patients with known HIV test results ranged from 12% (2007) to 95% (2015). This is in contrast to all other TB patients where HIV ascertainment varied from 89%-95%. ART uptake among paediatric TB patients was low at only 5% in 2007 and 50% in 2015. On other hand, ART uptake in all other patients has been increasing each year from 17% in 2007 to 92% in 2015. Treatment success rates have almost been similar to all other patients ranging between 79-88%, with concomitant low mortality rates (3-6%). Rates for lost to follow-up have been on the higher side (6-8%).

Conclusions and recommendations: Low uptake of HIV services among pediatric TB patients at KCH may be attributed, to poor coordination between TB and HIV clinics within the hospital and documentation problems. High rates of lost to follow-up may be due to lack of interest by TB clinic staff to follow-up children who are not coming for TB treatment. The NTP needs to put in measures to improve pediatric TB management in the country especially in central hospitals.

PD-842-28 Retrospective analysis of pediatric tuberculosis management at Kyiv City Pediatric Tuberculosis Hospital in Ukraine

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Background: Ukraine is currently listed by WHO as one of the high-burden MDR-TB countries in the world, with 9400 MDR-TB cases in 2014. Pediatric TB management in Ukraine is still maintained from Soviet-era policies including primarily hospital-based treatment. However, financial pressures and health restructuring will likely be

changing this model to more ambulatory care in the near future. We aimed to evaluate pediatric TB burden and current management in the Kyiv Region including the Kyiv City Pediatric Tuberculosis Hospital in Ukraine.

Methods: Data were collected on pediatric TB patients treated in the Kyiv Region including Kyiv City Pediatric TB Hospital from Jan 2012 to June 2015. Medical records were reviewed and demographic data, clinical presentation, HIV status, microbiological specimens, drug susceptibility testing (DST), contact DST, and treatment regimens were recorded. Duration of hospital stay and length of total treatment as well as treatment outcome was recorded. Descriptive statistics were applied.

Results: A total of 248 children were diagnosed and treated for TB in the Kyiv Region from January 2012 to June 2015. Sixty-six were between 0-4 years, 85 between ages 4-14, and 97 between the ages 15-18. Of these 248 children, only 37 had a positive microbiological specimen for TB. Twenty-two patients were diagnosed and treated for MDR-TB. All children remained hospitalized for the complete duration of their treatment with a range of six months to two years. All patients had successful treatment outcomes and no deaths were reported. Local and regional TB commissions composed of TB physicians discuss patient and clinical data prior to the initiation of any treatment regimens.

Conclusions: There is a significant burden of TB among children in the Kyiv region of Ukraine and an increasing number of MDR-TB cases. The current pediatric TB management system in Ukraine has excellent outcomes, however takes significant resources and also hospitalizes children for extensive periods of time, with a loss in socialization and family bonding necessary for normal development. With current planned health system changes, great care should be made to maintain good outcomes while also encouraging resumed life activities for children undergoing ambulatory TB treatment.

PD-843-28 Are young females more at risk? Three of four children were girls among notified pediatric MDR-TB cases in Maharashtra, India

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Background: Emergence of drug resistant tuberculosis is one of the major challenges faced by health community globally. Diagnostic and treatment services for multi-drug-resistant (MDR) TB patients started in 2007 in India under programmatic management of drug resistant TB (PMDT) component of Revised National TB Control Program (RNTCP). Tuberculosis is an important cause of morbidity and mortality among children in endemic areas. Little is known regarding epidemiology of pediatric tuberculosis and even far lesser information is available about epidemiology of drug resistant tubercu-

losis in children. This study is an attempt to document epidemiological characteristics of pediatric MDR TB patients notified to RNTCP in Maharashtra state of India.

Methods: In this retrospective study, we accessed data of notified MDR TB patients aged less than 15 years registered with RNTCP Maharashtra from the start of PMDT services in March 2007 till September 2014.

Results: There were 390 pediatric MDR TB cases notified in Maharashtra during the study period. Out of them, 300 (77%) were females. Median age of pediatric MDR TB patients among females was 13 years (IQR 11-14 Years) compared to 11 years (IQR 9-14 Years) among males. 51% of female pediatric MDR TB patients had given past history of anti-TB treatment compared to 34% male patients. 84% of female pediatric MDR TB patients had pulmonary TB compared to 68% males.

Conclusion: Major finding of our study was that three out of every four notified pediatric MDR TB patients were females. Female pediatric MDR TB cases had higher age, significantly high proportion of past TB episode and pulmonary site compared to males. Though potential causes of association between female sex and pediatric MDR TB is not known, this finding may be explained by cultural negligence of female child in study population, under-nutrition, poor immunity and poor past TB episode management. Further research is needed to identify the risk factors for MDR TB cases in pediatric females. Along with socio-demographic factors, immune mechanisms need to be studied to understand this epidemiology. This will help to develop policy and gender-sensitive interventions for prevention of MDR TB among young females.

24. Knowing the enemy (better): MDR epidemiology II

PD-844-28 Detection of XDR-TB in the Russian Federation

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Background: The Russian Federation is country with high burden of MDR-TB. Proportion of MDR-TB cases among new TB cases in 2014 was 19.0% and among retreatment cases: 49.0% and 15 585 laboratory-confirmed MDR-TB cases were registered. Regional TB bacteriological laboratories implemented DST of second line TB drugs (SLD) and increased its capacity for testing of MDR-TB patients to detect XDR-TB.

Methods: Regional laboratories DST data collection and processing was provided to calculate number of detected XDR-TB cases in 2014. For estimation of XDR-TB proportions in groups of TB patients we excluded data

from laboratories with insufficient coverage DST of SLD (>70% MDR-TB cases in each registration group).

Results: Total number of detected XDR-TB cases in Russia in 2014 comprised 3 211 or 17.0% out of all MDR-TB cases covered by DST of SLD. 1746 (54.4%) XDR-TB cases were detected in regions of European part of Russia and 1465 (45.6%) in Asian regions of Russia. Distribution of detected XDR-TB cases was: Siberia 728 (22.7%), Volga River geographical cluster 725 (22.6%), Russian Far East cluster 537 (16.7%), South of Russia and the North Caucasus 499 (15.5%), Nord West of Russia 356 (11.1%), Ural 200 (6.2%), Central Russia 166 (5.2%). Proportion of XDR-TB among new MDR-TB cases was estimated as 9.3%, among relapses 10.6%, among chronic patients 19.7%. Proportion of XDR-TB cases among new TB cases fluctuated from 4.3% in South of Russia and the North Caucasus to 16.4% in regions of Ural and among chronic TB patients, from 19.0% in South of Russia and the North Caucasus to 30.8% in Nord West of Russia.

Conclusions: XDR-TB is distributed in all geographical regions of Russia. Siberia and Volga River geographical clusters have 45.0% of all detected XDR-TB cases in Russia. Estimated proportion of XDR-TB among all detected MDR-TB cases in Russia is 17.0%.

PD-845-28 Multidrug-resistant tuberculosis in Brazil: descriptive analysis, 2010–2015

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Background: In the antibiotic era multidrug-resistant tuberculosis (MDR-TB, or resistance to isoniazid and rifampicin) is the newest threat for TB control and an important public health problem in several countries. An increase in MDR-TB cases is associated with high morbidity and mortality worldwide. The World Health Organization (WHO) estimated 480 000 new cases of MDR-TB worldwide in 2014. In Brazil 1232 cases of drug-resistant tuberculosis were notified in 2015. The study aims describe the characteristics of multidrug-resistant tuberculosis notified in Brazil over six years period, 2010 to 2015.

Methods: This was a study of routine data including all MDR-TB cases occurred in Brazil between 2010 and 2015 selected by treatment onset. We made a descriptive analysis of relevant sociodemographic variables such as sex, age, race, years of school and region of residence on the country. In addition, the proportion of Directly Observed Treatment (DOT), HIV test and type of resistance were described among these MDR-TB cases. The data were extracted from Information System for Tuberculosis Special Treatments (SITE-TB) and the analysis was performed with software Stata 12.

Results: A total of 3846 MDR-TB cases were notified in Brazil from 2010 to 2015. This number corresponds to

0.8 % of total TB cases notified in the period. During the studied period there was an increase in number of TB multidrug - resistant cases in the period of study. The results shows that most of these cases occurred among male (66.8%), in people aged between 18–39 years old (50.0%), non white (62.2%), with 4-7 years of school (38.0%), residents of the Southeast region of the country (42.1%). DOT was performed in most of them (78.1%) and in 78.5% the MDR-TB was acquired. Among 1654 MDR-TB cases tested by HIV, 14.2% (235) presented a positive result.

Conclusions: Multidrug-resistant tuberculosis is an important challenge to TB control. Our findings contribute with evidences to support the surveillance of multidrug-resistant tuberculosis in a country with high burden of disease, such as Brazil.

PD-846-28 Factors driving antibiotic resistance in a transitioning health system: results from the first multi-centre case-control study on tuberculosis in Myanmar

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Background: The emergence of approximately 480 000 multidrug-resistant tuberculosis (MDR-TB) cases annually is a particular threat for the populations of resource-limited countries. Although inadequate previous treatment has been identified as a major underlying cause of acquisition of resistance, there is limited evidence on factors associated with higher risk of MDR-TB in patients who have taken first-line anti-TB drugs. We investigate patient and health system related factors driving the emergence of MDR-TB in Myanmar, a setting where investment and reform are ongoing to reduce the high burden of both drug-sensitive and MDR-TB.

Methods: We conducted a multi-centre retrospective case-control study in ten townships health departments across Yangon. We included patients diagnosed between September 2014 and March 2015. Cases were 202 GeneXpert-confirmed MDR-TB patients with a history of prior first-line treatment for TB. Controls were 404 previously untreated smear-positive TB patients who had no known resistance to anti-TB drugs and had responded to first-line drugs at three months into treatment. Information on patients' demographic, socioeconomic, health status and behaviour was collected through face-to-face interviews and hospital record reviews.

Results: Multivariable logistic regression analysis indicated a higher risk of acquired MDR-TB in previously

treated TB patients with higher education (aOR: 1.78; 95%CI 1.01-3.13) and socioeconomic status (aOR: 1.99; 95%CI 1.09-3.63). TB patients with diabetes (aOR: 2.10; 95%CI 1.17-3.76) and those who missed first-line treatment more than once a week also had a greater risk of MDR-TB (aOR: 2.35; 95%CI 1.18-4.65). Patients who had a close contact diagnosed with MDR-TB or one that died of TB in past five years also experienced a greater risk of developing MDR-TB.

Conclusions: Coinciding with a surge in funding to improve health in Myanmar, this study provides new information about programmatic factors that can be addressed, and TB patient groups that can be prioritised, to prevent emergence of MDR-TB. Specifically, the study indicates that TB patients who experience frequent short interruptions in treatment and those with diabetes may require enhanced treatment support and monitoring in order to prevent acquisition of drug resistance.

PD-847-28 Burden of multidrug-resistant TB in Indian states: current trend

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Background: As per WHO, India has the highest TB burden (23%) globally and the estimated percentage of new cases with Multi-drug Resistant TB (MDR-TB) is 2.2. In 2013 about 35,400 people were diagnosed with MDR-TB and 20 763 were treated under Revised National TB Control Programme (RNTCP). Reports indicate that MDR-TB prevalence is very high in some pockets of the country. This paper analyses the trends of MDR-TB and related mortality from the available data in Indian states from 2009 to 2015.

Methods: MDR-TB data from 2009 to June 2015, of 35 Indian States and Union Territories is collected from many documents. Main sources were Parliamentary question-answer session documents. Various reports on MDR-TB from the ministry, Evaluation reports, Annual reports of RNTCP, WHO reports, newspaper reports from various parts of the country etc. were considered for analysis and the trends of disease burden and related mortality in each state studied.

Results: MDR-TB cases and related deaths in India are increasing. Until June 2015, RNTCP has diagnosed 72 196 MDR-TB patients between 2012 and 2015. From 2009 to 2012, mortality from MDR-TB reported is 4515. In 2009, total deaths were 238, but in 2012, it increased up to 3029. Similarly, State of Maharashtra registered the highest number of MDR TB cases (15 909) and a thousand people died. In 2012, there were only 110 cases in State of UP, but by 2014, it increased up to 2798 cases and in 2015, it reached 2255 by June itself. More than 85% of the Indian states are showing an increasing trend between 2012-14, Karnataka (714%), Bihar (722%), Haryana (345%), Sikkim (145%) etc. whereas Kerala showed a declining trend.

Conclusions: MDR TB services cost about 30-40% of the entire TB budget. Initiating Drug Susceptibility Test (DST) in the high incident pockets is a priority. Reasons for the apparent concentration of the disease in certain pockets needs to be explored.

PD-848-28 Anti-tuberculosis drug resistance survey in Iraq

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Background: Tuberculosis is a serious disease that is endemic in Iraq. Iraq lacks precise estimates for the burden of its severe forms drug resistant tuberculosis (DR-TB) particularly multidrug-resistant TB (MDR-TB). **Aim:** To measure the prevalence of DR-TB among new and previously treated smear positive pulmonary TB cases in Iraq.

Methods: Iraqi National Tuberculosis Control Program conducted a cross-sectional national study selected patients using random cluster sampling. Patients were new and retreated pulmonary tuberculosis patients (sputum smears positive for acid fast bacilli) enrolled immediately upon detection during November 2013 to December 2014. Demographic and clinical data collected through direct interviews. Laboratory methods were direct smear microscopy to detect AFB in sputum, culture and drug susceptibility testing on solid media. STATA was used for data analysis. The χ^2 test was used to test the significance of association between variables. Logistic regression used to study causal associations. Both weighing cases and imputation preceded proportions estimation and odds ratio.

Results: Significant findings were: retreatment associated with male sex and age groups 25-43 and 55-64 years. MDR-TB constituted 1.1% (0.3-1.5%) of new TB patients and 19.7% (12.5-26.8%) of retreatment TB patients. Regression analysis revealed that retreatment (particularly after relapse), and history of diabetes mellitus are risk factors for MDR-TB in Iraq. INH resistance is (7.6%) and rifampicin resistance is (5.9%). **Conclusion:** Iraq is a country with a low MDR-TB level.

PD-849-28 Unravelling TB drug resistance in Kenya

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Background: Monitoring of resistance to drugs used to treat tuberculosis is an important exercise both globally and locally. Urgency in this area has been accelerated due to development of strains that can compromise national and international security. The overall goal of the survey was to assess TB drug resistance situation in Kenya.

Methods: The survey used World Health Organization recommended methods which included a cross-sectional study design targeting all new and previously treated smear-positive TB patients in 50 randomly selected clusters. All specimen collected were transported overnight to the National TB reference laboratory where Ziehl Neelsen test was performed, GeneXpert, solid and liquid cultures and results read and reported appropriately. Quality Assurance was done by Supranational National Laboratory in Brisbane, Australia. There was 100% concordance in results..

Results: A total of 2171 eligible participants were recruited into the survey consisting of 1910 new cases, 258 previously treated cases and 3 uncategorized participants. Male to female participant ratio was 2:1. From 2168 specimens, 11 (0.5%) non tuberculous mycobacteria (NTM) were isolated (7 from new and 4 from previously treated patients), 90 contaminated (4.2%), 182 culture negative (8.4%), 1,885 culture positive (87%). Drug susceptibility testing (DST) was done on 1876 samples (1680 new cases and 194 previously treated cases). A total of 15 MDR cases were identified, 11 from new cases (0.65%) and 4 from previously treated TB cases (2.06%). Rifampicin resistance for new cases was 1.3% (95%CI 0.8-2.0) while INH resistance among new cases was 5.5% (95%CI 4.5-6.7%).

Conclusions: There is a low level of MDR-TB especially among new TB cases (0.65%) and a higher level in the previously treated cases (2.06%). These results imply a previously well-functioning Directly Observed Treatment Short Course (DOTS) program which should be strengthened and enhanced. The survey confirmed presence of NTM, albeit low levels (0.5%). Cumulatively, these figures are going to grow and the TB program needs to develop methods to address the challenge. In a country with a huge TB-HIV burden, NTMs are going to pose increasing challenges over the years.

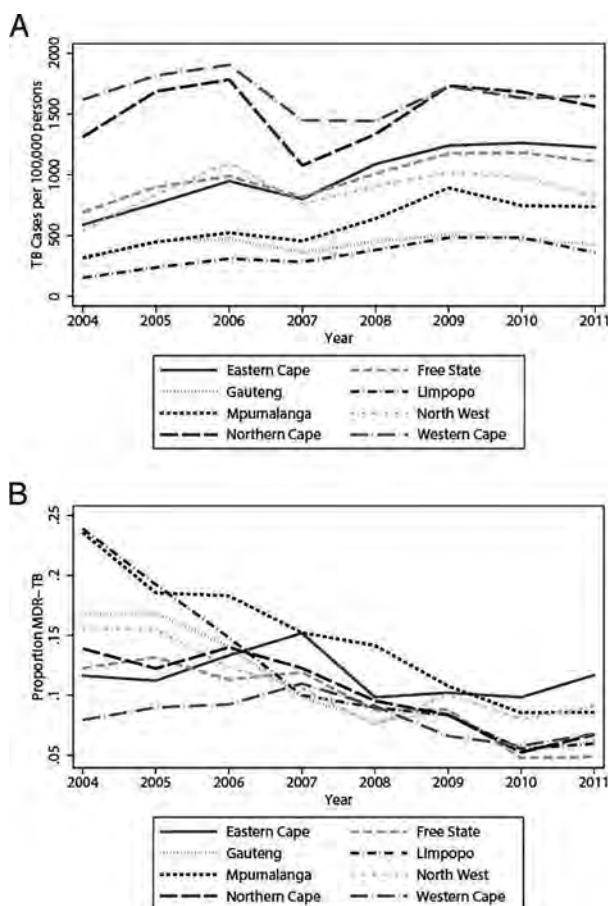
PD-850-28 Trends in tuberculosis and multidrug-resistant tuberculosis among provinces in South Africa

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Tuberculosis (TB) is the leading cause of infectious disease deaths worldwide, responsible for an estimated 1.5 million deaths each year. The burden of disease is further compounded by the development of multidrug-resistant TB (MDR-TB), a growing public health concern. Identifying trends in TB incidence, MDR-TB incidence, and the proportion of TB cases characterized as MDR is a priority action for high burden countries such as South Africa where approximately 450 000 new cases of TB developed in 2014 and the proportion MDR-TB has reached 39% in certain regions. We used data

from the National Health Laboratory Service database to estimate the annual incidence rate of TB and MDR-TB, adjusting for age and sex, and the proportion MDR-TB for each province of South Africa. Data include all TB-positive test records from patients aged 16-64 years collected in 5122 public health facilities from January 2004 to December 2011, the period before the introduction of routine Xpert testing. KwaZulu-Natal province was excluded from analysis due to limited data availability. Our results indicate an increase in TB incidence between 2004 to 2009 in all provinces except Western Cape before leveling off between 2009 and 2011. The burden of TB remains high in all provinces. By contrast, the proportion of MDR-TB steadily decreased while the incidence rate of MDR-TB increased in all provinces between 2004 and 2011. These trends suggest the drop in proportion MDR-TB is likely driven by a relatively large increase in the incidence of TB rather than a decline in MDR-TB incidence.

Figure A) TB incidence, B) Proportion MDR-TB, South Africa, 2004–2011



PD-851-28 Strengthening multidrug-resistant tuberculosis surveillance program in the Arctic area of Russia using novel technologies for detecting the causative agent

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Background and challenges to implementation: Sakha Republic (Yakutia) is the largest subnational entity in the world, with an area equal to one-fifth of the territory of Russia, with 40% of its area lying in the high Arctic zone, with low population density. There are 34 rural regions, wherein medical care is provided via central hospitals and small medical stations. Average TB incidence is 70 per 100 000. The Center for TB provides centralized diagnosis by receiving patients and by examining diagnostic material shipped from remote regions. We aimed to study the impact of novel drug sensitivity testing technologies on treatment effectiveness in 2 patient cohorts with multidrug-resistant (MDR) TB (years 2009 and 2013).

Intervention or response: BACTEC test system was introduced in 2010, and novel MTB DNA detection technologies (Xpert MTB/RIF and real-time PCR) were implemented in 2013.

Results and lessons learnt: 2009 cohort comprised 559 new patients with TB, 88% of whom had been diagnosed by standard solid medium test. MDR TB was detected in 63 patients; time to detection was 1.5 to 3 months. Before being started on proper regimen IV, patients had been receiving standard regimen I, consisting of only first-line drugs, for a long time. At the end of a 24 month course, treatment outcomes were: 68.3% cured; 11.1% failed; 17.5% died; 3.1% transferred out. Cohort 2013 included 591 patients, diagnosed mostly by liquid medium BACTEC method. 98% of patients were covered by diagnostic test, and MDR-TB was detected in 98 patients. In some patients, sputums were additionally tested for resistance to rifampicin (as a marker for MDR) using Xpert MTB test, and for mutations in *rpoB* gene (resistance to rifampicin) and *katG* and *inhA* genes (resistance to isoniazid). Time to detection of MDR shortened to 2-3 weeks using BACTEC, and to 1-2 days using molecular genetic methods. Outcomes were: 81.6% cured; 7.2% failed; 6.1% died; 5.1% transferred out.

Conclusions and key recommendations: The use of molecular genetic techniques for the diagnosis of MDR-TB patients contributes to case identification, improved treatment, conducting anti-epidemic measures during outbreaks, strengthening TB infection-surveillance program, despite the climate and geographical conditions.

PD-852-28 Nationwide anti-tuberculosis Drug Resistance Survey (DRS), the Republic of Azerbaijan, 2012–2013

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Background: Azerbaijan is a high tuberculosis (TB) priority country in the WHO European Region where 22% of new and 56% of retreated TB cases are multidrug-resistant (MDR). The goal of this survey was to assess the prevalence and risk factors for MDR-TB and make recommendations to reduce the burden of MDR-TB in Azerbaijan.

Methods: A cross-sectional survey was conducted between October 2012 and April 2013. Study included 549 new and 240 retreated patients >15 years of age. The latter included cases which had deteriorated after improvement, treatment failures, non-standard regimens and patients arbitrarily interrupt treatment. Diagnostic procedures included sputum microscopy, culture identification, drug susceptibility testing to first (Rifampicin, Isoniazid, Ethambutol, Streptomycin) and second-line (Ethionamide, Ofloxacin, Para-Aminosalicylic Acid, Cycloserine, Amicacin, Capreomycin) drugs.

Results: 231 (42%) of new and 146 (61%) of retreated patients were resistant to ≥ 1 drugs; 72 (13%) of new and 66 (28%) of retreated cases were resistant to RMP and INH. Amongst MDR-TB cases, 27 (38%) of new and 31 (47%) of retreated cases had pre-XDR/XDR-TB (resistant to RMP, INH, FQS, and injectable drugs). In those with treatment failure, 38 (51%) had MDR/XDR-TB which was fifteen times higher than found in relapse cases (RR = 15.2, 95%CI 6.0-39). A history of imprisonment was significantly associated with new cases of MDR/XDR-TB (RR = 3.4, 95%CI 1.1-10.4). Retreated patients also had high risk for MDR/XDR (RR = 2.7 95%CI 1.0-7.0).

Conclusions: Azerbaijan remains a high MDR-TB burden country. Risk factors including retreatment, treatment failure, and imprisonment contribute to MDR/XDR TB problem. We recommend standard interventions including psychosocial support to improve adherence to treatment and mandatory TB drug resistance testing.

PD-853-28 Acquired drug resistance among culture-confirmed tuberculosis cases in England, Wales and Northern Ireland: a retrospective cohort study, 2000–2014

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Background: The Collaborative Tuberculosis Strategy for England 2015–2020¹ outlines several action areas for TB control, one being reduction of drug-resistant TB. Resistance acquired while on treatment represents a failure somewhere in the patient-treatment pathway, and

poses a risk for drug-resistant TB transmission. This study aims to describe the frequency, timing of, and factors associated with acquired resistance among TB cases in England, Wales and Northern Ireland (EW&NI). **Methods:** We conducted a retrospective cohort study of culture-confirmed TB cases notified in EW&NI from 2000–2014. Acquired resistance was defined as resistance on repeat culture, following a sensitive result for the same anti-TB drug. A descriptive comparative analysis of demographic characteristics and outcomes between TB cases with and without acquired resistance was conducted.

Results: Of the 65 126 culture-confirmed TB cases, 148 (0.2%) acquired resistance to at least one anti-TB drug; most frequently to rifampicin (49, 0.08%) and isoniazid (46, 0.07%). When testing occurred, 22 cases acquired resistance to at least one second-line drug. The median time between starting treatment and acquiring resistance was 92 days (IQR 31–264). A higher proportion of TB cases with acquired resistance were aged 15–64 years (96%), born in Lithuania (7%), China (6%), or South Africa (5%), and had a social risk factor (prison, alcohol use, drug use or homelessness) (21%) compared to those without acquired resistance ($n = 64\ 978$, 84%, 0.5%, 1%, 2% and 11% respectively). A high proportion of cases with acquired resistance had died (7%) or lost to follow-up (7%) as the final reported outcome.

Conclusions: There is little literature available on acquired resistance among TB cases but in a low-incidence country, it is important to focus control efforts on risk groups. This study shows acquired resistance is low in EW&NI, but highlights risk groups more likely to acquire resistance including those with a social risk factor and born in certain countries. This information can be utilised by clinicians treating TB patients in EW&NI to identify those at risk of acquiring resistance and alter drug regimens rapidly when the acquisition of resistance occurs.

Reference

¹Public Health England, National Health Services. Collaborative Tuberculosis Strategy for England 2015–2020. London, UK: Crown, 2015. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/403231/Collaborative_TB_Strategy_for_England_2015_2020_.pdf Accessed August 2016

PD-854-28 First survey of anti-tuberculosis drug resistance in Djibouti, 2014

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Background: Djibouti, a small country in the Horn of Africa with a population of <1 million has one of the

highest estimated tuberculosis (TB) incidence of the continent (619/100 000 pop in 2014). In recent years, its national TB programme (NTP) has introduced state of the art molecular diagnostics through the support of EXPAND-TB to enhance the local capacity to detect and treat TB patients. Nonetheless, treatment success has been suboptimal (75% in new and relapses in 2013 cohort). Concern about the emergence of drug resistance led the NTP to undertake their first national drug-resistance survey in 2014-2015.

Intervention: The survey aimed to estimate the proportion of new and previously treated patients with multidrug-resistant (MDR) TB in a representative sample of TB patients presenting for care. Patients were consecutively enrolled from diagnostic centres across the country until reaching the required sample size. Sputum samples were tested by Xpert MTB/RIF and those with rifampicin resistance underwent phenotypic testing to determine susceptibility to first line anti-TB drugs. Bacterial isolates were sent to the supranational TB reference laboratory (SRL) Milan, Italy, for external quality assurance. These strains underwent whole genome sequencing analysis to identify mutations causing resistance to pyrazinamide, fluoroquinolones and second-line injectables. Genotypic cluster analysis of rifampicin resistant cases was performed to provide epidemiological insights on strains transmission.

Results: 301 new and 66 previously treated TB cases were enrolled between September 2014 and March 2015. A total of 33 cases had MDR-TB, at 4% among new and 31% among previously treated cases. Among MDR-TB patients, 59% were resistant to pyrazinamide and 19% to all second-line injectables but none had fluoroquinolone resistance.

Conclusions and key recommendations: Levels of MDR-TB in Djibouti are similar to those detected in a survey in neighbouring Somalia in 2011. Results imply that among pulmonary TB cases notified each year in Djibouti, about 100 MDR-TB cases would occur. The absence of resistance to fluoroquinolones bodes well for the response to treatment with second-line treatment regimens in these patients although resistance levels for pyrazinamide suggests that this drug may not be effective in the majority of MDR-TB patients.

25. 'With a little help from my friends': linking the public-private sectors

PD-855-28 Implementation of Public-Private Mix for TB control in India: perspectives and practices of district managers and frontline workers

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Background: Public-Private Mix (PPM) have been a core component in the TB control strategy in India. However, ensuring the effectiveness and sustainability of PPM still constitutes one of the major challenges for the future. The Revised National TB Control Programme (RNTCP) encourages District TB Officers (DTOs) and Frontline TB Workers (FTWs) to actively involve Non-Government Organisations (NGOs) and Private Practitioners (PPs) to improve the quality of front line service delivery. It is these actors who are capable of re-shaping policy during its implementation, thus highlighting the importance of studying their behaviour. The paper reports the findings from an empirical study on the perspectives and practices of public sector actors towards implementation of the PPM-TB strategy in India.

Methods: The study was carried out between November 2010 and December 2011 in a district of a southern Indian State and utilised qualitative methodologies, combining observations, informal interactions and 26 in-depth interviews with public sector actors. The data was coded, and analysed using thematic analysis.

Results: The guidelines for the involvement of PPs and NGOs highlight the crucial role of the DTOs and FTWs in building and maintaining sustainable partnerships. In principle, DTOs and FTWs approved of the PPM-TB policy, however, in practice they took a negative stance towards NGOs and PPs. DTOs indicate that NGOs and PPs were 'individual bodies, more autonomous, and not working under the control of the district TB office'. FTWs asserted NGO practices to be 'autocratic' in nature, and expressed negative opinions of PPs TB management practices, describing them as 'misleading patients', 'not revealing TB status to patients', 'doing unnecessary tests', 'not doing regular monitoring', and 'prescribing incomplete treatment'. These conflicting perceptions held by DTOs and FTWs were not only deeply rooted within their mind-set, but were reflected directly and indirectly in their routine practices.

Conclusions: This paper draws attention to the perceptions and opinions frontline actors from the public sector had towards NGOs and PPs, demonstrating misinterpretation and misalignment of the policy in practice. If national policies are to be effective at the district and sub-district level, then the implementers need to have appropriate information and adequate training.

PD-856-28 Outcomes of institutionalizing DOTS in urban settings on tuberculosis case notification and treatment: the case of Kandahar city

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Background: Afghanistan encompasses 2400 public health facilities and many private practitioners, clinics and hospitals. Kandahar has 72 public facilities, one prison, 13 private hospitals, 410 pharmacies, and 320 private practitioners. Private sectors usually do not apply Ministry of Health procedures that resulted in low TB case notification in Kandahar. The objective was to evaluate outcomes of urban DOTS implementation on TB case notification and treatment in Kandahar.

Intervention: In Jun 2015, NTP introduced urban DOTS approach to stakeholders and provincial health team and launched Urban DOTS in five private hospitals, one public hospital, and a prison. TB services delivery institutionalized at these facilities: nurses, doctors, and lab-technicians were trained on TB case detection and treatment and standardized recording and reporting forms. Also, NTP supplied drugs and reagents, and executed supportive supervision. TB data of 2014 from 30 health facilities was compared to data of 2015 from seven urban DOTS covered facilities.

Results and lessons learnt: In 2015, 11 134 individuals attended seven urban DOTS facilities. They identified 542 (4.86%) presumptive TB patients, and diagnosed 53 (10%) bacteriologically confirmed, 167 (31%) all forms TB cases and initiated treatment. Case notification for bacteriologically confirmed and all forms TB cases was 476 and 1463 in 100 000 outpatient attendance (OPD) attendees, respectively. While, in 2014, 480 226 OPD attended 30 public facilities that notified 8919 (1.9%) presumptive TB patients, diagnosed 660 (7%) bacteriologically confirmed, and 1349 all forms of TB cases. TB case notification for bacteriologically confirmed and all forms of TB cases was 137 and 281 in 100 000 OPD attendees.

Conclusion and recommendations: Urban DOTS implementation resulted in three-fold improvements in presumptive TB case identification and case notification for bacteriologically confirmed and five-fold increase for all forms TB cases in intervention facilities. We recommend expansion of urban DOTS to similar settings in Afghanistan and elsewhere.

Table 1: Comparison of key TB variables between intervention and control areas

Variable	Intervention area (7 facilities, 2015)	Control area (30 facilities, 2014)	Tests of significance: p-value
Outpatient attendance (OPD)	11,134	480,226	
Number of presumptive TB cases	542	8,919	P < 0.01
Presumptive TB patient identification rate	4.9%	1.9%	
Total number TB cases diagnosed (All forms)	163	1,349	P < 0.01
Number of bacteriologically confirmed TB cases diagnosed	53	660	P < 0.01
Number of all forms of TB cases notified per 100,000 OPD attendees	1463	281	P < 0.01
Number of bacteriologically confirmed TB cases notified in 100,000 OPD attendees	476	137	P < 0.01

PD-857-28 Tuberculosis case notification by private practitioners in Delhi, India: is the mechanism sustainable?

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Background: In May 2012, the Revised National Tuberculosis Control Program (RNTCP) of India made TB notification mandatory from private practitioners (PP). To ease TB notification RNTCP developed the case based web based online reporting mechanism called 'Nikshay'. However, the support from private health sector towards TB notification was sub-optimal as there were operational issues in reporting mechanisms. Hence we conducted a study to understand the implementation issues from the perspective of private practitioners and program personnel engaged in TB notification.

Methods: Cross-sectional qualitative study was conducted in two tuberculosis districts of Delhi. The selection of PP was drawn from the list of Nikshay registrations during January 2014 to April 2015. We conducted in-depth interview of 30 practitioners of which 19 were private practitioners and 11 were program personnel from RNTCP. Grounded theory was used to conceptualize the latent social patterns and structures involved in implementation process and related challenges. The challenges conceptualized as themes from interviews of private practitioners were: 1) incomplete address details given by patient, 2) non-availability of human resource at health center, 3) insufficient knowledge in computer handling. The challenges as revealed by program personnel were: 1) Low salary and motivation among tuberculosis health visitors, 2) busy schedule of higher cadre officials with RNTCP, 3) Sub-optimal data collection mechanisms. Atlas Ti (version 6.0) was used to analyse the data.

Results: Challenges faced by the private practitioners were at multiple levels. They were mainly due to the

backlash of poor planning and implementation of notification process at state and district level. The mechanism of notification through website was complex and not fully equipped to validate the entries made. The private practitioners have not experienced any gains either individually or to their patients upon notification. Program could not prioritize the advocacy on the importance of TB notification and eradicate various myths prevailed among the private practitioners on TB notification.

Conclusions: An advocacy forum needs to be developed at National, State and district levels to promote TB notification. Emphasis of the program should be concentrated on convincing the practitioners on the importance of TB notification.

PD-858-28 Tuberculosis management practices of private practitioners in Central India

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Background: Private sector accounts for 82% of all outpatients in India, with no significant variations by income group (Mishra et al, 2003). Private Practitioners (PP) in India treat a substantial proportion of the Tuberculosis (TB) cases. Though Government of India declared Tuberculosis a notifiable disease on 7 May 2012, notification from private sector is minimal. Also limited information is available on TB management practices of PPs or on efficacy of India's Revised National Tuberculosis Control Program (RNTCP) to improve quality of TB management through training of PPs.

Methods: A cross-sectional survey was conducted through systematic random sample of 104 Qualified PPs in urban areas of Central India (Madhya Pradesh) using self-administered questionnaire. We presented sample clinical vignettes and determined proportions of PPs who reported practices consistent with Standards for TB Care in India (STCI). Information was collected about their involvement and reasons for non-involvement and association between RNTCP training and adherence to STCI.

Results: Amongst the PPs interviewed, only 36.5% are treating TB patients; of which 55% preferred Chest X-ray to sputum examination for TB diagnosis. Amongst these PPs who are treating TB patients, only 42% are notifying TB patients in the Government of India portal. Only 65.8% PPs, who are treating TB patients, are aware that TB is a notifiable disease and it is mandatory to notify every TB patient; others felt that they might lose their patients in case they notify them. For new pulmonary TB patients, 42.1% of provider responses were consistent with STCI guidelines, and 57.9% of responses were non-consistent. RNTCP training was associated with diagnostics or treatment practices. Only 15.4% PPs who were interviewed have been sensitised on STCI. Majority (58%) expressed no faith in RNTCP and expressed that documentation in RNTCP was too

difficult. Majority PPs (81%) expected appreciation by Government as a way of increasing their involvement.

Conclusions: There is an increasing need for dissemination of STCI amongst all providers who are managing and/or treating TB cases. Efforts to achieve universal access to quality TB management must account for the low quality of care by PPs and lack of demonstrated effect of current training efforts.

PD-859-28 Large-scale private provider engagement via e-health and free TB drugs in urban Patna, India

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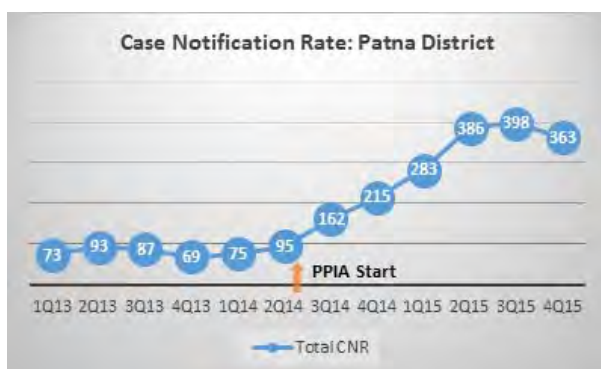
Background: Private sector providers (PP) dominate health care in India but are characterized by sub-standard diagnostic and treatment practices, high patient costs, low treatment completion rates, and inadequate coordination with public sector TB programs. We piloted an urban PP Interface Agency (PPIA) strategy, facilitating private provider TB notification and providing free diagnostic and anti-TB treatment via user-friendly e-health systems.

Intervention: In Patna District, Bihar, private sector doctors, pharmacies, and diagnostic facilities were mapped and prioritized for PPIA engagement. PPIA field staff systematically engaged PP, facilitating TB notifications and e-vouchers for free radiography, smear microscopy, Xpert MTB/RIF, and anti-TB drugs as per national standards. Patients redeem vouchers at private diagnostic centers and pharmacies, who validate via SMS/mobile. Patients receive adherence support with self-reporting via call centre, reminders, and active follow-up in case of non-reporting or missed refills.

Results: Between July 2014 to February 2016, 1603 doctors were mapped, 875 targeted, and 627 (72%) engaged. 544 doctors (45%) notified TB cases in February 2016. Total TB case notification rate (from public and private sector) nearly quadrupled in 2015 as compared to 2013, prior to PPIA. (Figure). The increase was driven by private TB notification while public TB notification remained stable. Approximately 55 % of private TB treatment was covered by PPIA notifications and support system, as measured by surveillance of private anti-TB drug sales. Among 5595 TB patients from cohorts of 2Q 2014-1Q 2015, 75% successfully completed treatment with PPIA adherence support and monitoring. 474 cases of rifampicin-resistant TB were detected and transferred to public sector care.

Conclusions: The basic model of extending public services to private providers via PPIA and e-health systems proved highly effective, dramatically advancing TB control in Patna district. Similarly, private sector TB care quality can be improved across India with cost-optimization and scale-up of services.

Figure Patna District CNR



PD-860-28 Models of corporate engagement in TB control in India

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Background and challenges to implementation: Corporate sector with its pool of resources, management skills and reach among workers/ communities can play a vital role in TB control efforts. We here describe the experience of corporate engagement through The Challenge TB project in India.

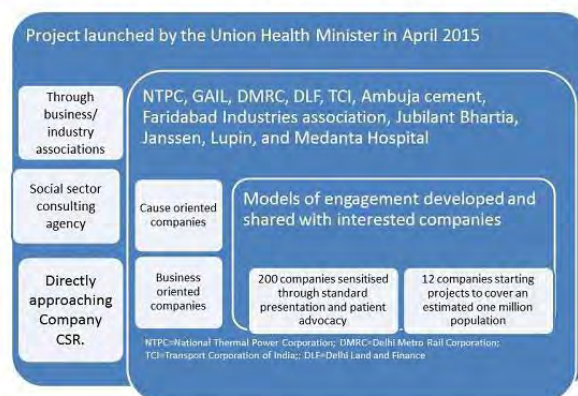
Intervention or response: Challenge TB launched The Call to Action for a TB-free India to mobilize a wide range of stakeholders. Corporates/businesses were identified as a key stakeholder for CSR and workplace interventions on TB. A corporate strategy was developed identifying high risk industries, industries with a large workplace and Industries having interventions in health. To sensitize them on TB, a three pronged approach was used for outreach: a. Through business/ industry associations, b. Through social sector consulting agency, c. By directly approaching Company CSR.

Results and lessons learnt: Over 200 corporates were mapped and sensitized through a mix of the above approaches. 12 corporates finally agreed to initiate CSR and workplace intervention projects on TB. Around one million people are expected to be covered through such activities by corporates. The above strategy and outreach effort has provided a framework for corporate engagement that can be replicated and is shared in the Table.

Conclusions and key recommendations: Involvement of corporate sector in TB showed positive results in terms of CSR commitments and workplace projects on TB. While business association were useful in sensitizing a huge number, one on one engagement with sensitized company CSR managers resulted in commitments.

Figure Process of corporate engagement

Process of corporate engagement



26. Tuberculosis and diabetes outcomes: not always 'so sweet'

PD-861-28 Treating diabetes in tuberculosis patients: experience with metformin and insulin in the TANDEM Program

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Background: Diabetes (DM) is common among tuberculosis (TB) patients, but data regarding DM management in TB patients are scarce. Most guidelines recommend insulin in TB patients, but metformin, a first choice drug for DM, gives no hypoglycemia, has a lower cost, and is easier to use. We report our experience with metformin and insulin in an ongoing pragmatic clinical trial in the TANDEM program (www.tandem-fp7.eu) in Indonesia.

Methods: In this trial, patients are allocated to standard or intensive arm, by means more intensive glucose monitoring with adjustment of DM medication; we only analysed data from subjects allocated to intensive arm. DM treatment was according to the flowcharts, mostly using metformin as an initial DM drug. Metformin was titrated until target blood glucose was achieved (maximum 2550 mg/day). For newly diagnosed diabetes, metformin were delayed one week after starting TB treatment. Metformin was given with meal at least 2 hours after taking TB drugs. Insulin was given according to the average value of self-monitored blood glucose values.

Results: From 47 TB-DM patients recruited so far, 68% had known DM, and 33 (70%) were treated with metformin, either alone or in combination with insulin, at a dose of 500-2550 mg daily. Of 33 patients, 29 (88%) experienced at least one side effects, including nausea (88%), vomiting (70%) and diarrhea (18%). They were mostly mild and occurred within 2 weeks after starting metformin. One patient taking metformin 500 mg b.i.d died with suspected lactic acidosis. With regard to insulin, 57% of patients had an indication for Insulin, but one-third of them refused, while hypoglycemia occurred in more than one third of those starting insulin, mainly due to incorrect use of insulin.

Conclusions: DM treatment using metformin in TB-DM patients leads to frequent side effects; some of which may overlap with those of TB medication, and may be serious. Insulin was often not accepted and frequently led to hypoglycemia in TB patients. These data highlight some of the challenges of DM management in TB patients, and underline the need for more study.

PD-862-28 Impact of diabetes on drug-resistant tuberculosis treatment outcomes: retrospective cohort study in Pakistan

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Background: Diabetic patients have altered immunity which makes them susceptible to different types of infections, notably tuberculosis. Few studies have investigated the impact of diabetes mellitus (DM) on treatment outcomes with drug-resistant tuberculosis (DR-TB) particularly in the context of developing countries like Pakistan. The present study was designed to analyze the treatment outcomes of DR-TB patients with respect to the presence or absence of diabetes as comorbidity.

Methods: A retrospective cohort study was carried out including all DR-TB patients enrolled at all programmatic management of drug resistance tuberculosis (PMDT) treatment sites of Pakistan between 2010 and 2013 with known treatment outcomes. Medical records were retrospectively reviewed for demography, TB treatment history, comorbidities, AFB cultures and drug susceptibility test (DST) results, treatment modalities and outcomes. Patients will be considered diabetic if they had a previous history of DM and are using insulin and/or oral hypoglycemic agents at the time of DR-TB diagnosis. The data of 122 DR-TB patients with DM and 1881 DR-TB patients without DM were analyzed in the study.

Results: Gender and social status were not significantly different in DR-TB patients with or without DM. The cure and treatment completion rates are slightly better in DR-TB patients with DM (66% and 2%) than in DR-TB without DM (62% and 3%). Death rate is almost equal in DM and Non-DM patients (16% and 15% respectively). Similarly, treatment failure rates and lost to

follow up is not significantly different in DM (3% and 4%) and Non-DM patients (4% and 5%) with DR-TB.

Conclusions: No significant difference in treatment outcomes was found in DR-TB patients with and without diabetes.

PD-863-28 Epidemiological characteristics and treatment outcomes among Peruvian MDR-TB patients with and without diabetes

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Background: Among the Latin American countries, Peru reports a high incidence of Tuberculosis (TB) and a high incidence of multidrug-resistant tuberculosis (MDR-TB), mostly in the capital city of Lima. Diabetes (DM) is also increasing, specifically in urban areas in Peru. This context where MDR-TB and DM collide, there is not adequate evidence on epidemiological situation on Peruvian MDR-TBDM patients

Methods: MDR-TB electronic records from the Peruvian National TB Program operational patient's database were reviewed. Adult patients who started MDR-TB treatment between 2010-2014 in Lima were included in the study. We evaluated TB treatment outcomes and their associate factors among MDR-TB patients with DM (MDR-TB/DM) and MDR-TB patients without DM (MDR-TB). Good treatment outcome (GTO) was defined as cured and/or completed, and poor treatment outcomes as death, abandoned treatment or relapse. Prevalence Ratios (PR) were calculated using Poisson regression.

Results: 1829 patients were included in the study, 66.9% were male. The median age was 27 (IQR 22-36); 28.2% were over 35 years. Median BMI was 21.7kg/m² (IQR 19.5-24.1); 19.4% had a BMI >25kg/m²; and HIV prevalence was 3.6%. The overall prevalence of DM among MDR-TB was 6.3% (95%CI 5.3%-7.6%), but DM prevalence increases with age: 18-25 years (0.4% 95%CI 0.1%-1.3%); 25-34 years (1.8% 95%CI 1.0%-3.2%); 35-44 years (7.2% 95%CI 4.5%-11.3%); 44-54 (29.0% 95%CI 22.1%-36.9%); and over 55 years (31.4% 95%CI 24.1%-39.7%). There is not difference in proportion of male patients among MDR-TBDM and MDR-TB (62.1% vs. 67.2%; $P=0.3$), but MDR-TB/DM had higher proportion of patients with BMI >25kg/m² (36.2% vs. 18.3%; $P < 0.001$). The frequency of GTO was 53.5% and 59.02% among MDR-TB/DM and MDR-TB respectively ($P=0.1$). The frequency of death was higher among MDR-TB/DM compared with MDR-TB (18.1% vs. 7.7%; $P < 0.01$), however, the significance of this association declined after adjustment for BMI, age, gender and cavitations (PR=1.3 95%CI 0.9-2.0; $P=0.2$)

Conclusions: MDR-TB/DM patients are generally older, more overweight/obese and tend to have worse TB treatment outcomes, specifically death. Prospective studies exploring the role of glucose management among MDR-TB/DM patients including HbA1c levels during treatment are required to have a better characterization of this population.

PD-864-28 Comorbidities and other factors associated with retreatment of tuberculosis in Brazil, 2010–2014

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Background: Among the problems arising from the failure of tuberculosis treatment, the retreatment, by the premature discontinuation of medication or relapse, is frequent and potentially a drug resistant tuberculosis case. This study aims to analyze comorbidities and other factors associated to retreatment of tuberculosis in Brazil, 2010–2014.

Methods: This is a descriptive study, historical series, conducted with 59 981 TB cases in retreatment, representing 14.5% of TB patients notified in the national information system in the 2010–2014 period. Were evaluated sociodemographic variables (gender, age, education and race/ color), clinical form (pulmonary, extrapulmonary), sputum smear results, comorbidities and other situations of vulnerability and closing of cases.

Results: Most cases of retreatment were in men (73.2%), in the age group of 30 to 39 years (27.7%), mixed race (47.5%) and less than eight years of study (50.5%). Relapses in Brazil contributed with 6.8% and returns after lost to follow up with 7.7%. Regarding institutionalized patients 72.7% were inmates. Considering the clinical form, 89.9% of patients had pulmonary form of the disease. About the diagnosis of sputum smear microscopy among pulmonary cases, 90.5% had one sample realized (63.7% positive and 26.8% negative) and 48.8% had two samples (33.2% positive and 15.6% negative). The HIV testing had 27.7% positive results. Regarding comorbidities: 21.4% had SIDA, 5.4% diabetes mellitus and 3.1% mental illness. With regard to situations of vulnerability: 28% were alcohol abusers, 26.1% were using illicit drugs and 20% were smokers. In closing, the cure rate was 52.1%, lost to follow up 27.5% and the death 4.2%.

Conclusions: The retreatment cases in Brazil are a critical problem, with high rates of comorbidity with SIDA, lost to follow up and deaths. There is also a high proportion of alcoholics and injecting drug use, demonstrating the need for joint monitoring with the mental health and psychosocial support. In this group it is important extend the surveillance of cases as a strengthening strategy of the disease control in the country.

PD-865-28 The influence of diabetes mellitus on treatment outcomes of patients with pulmonary tuberculosis

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Background: To investigate the impact of Diabetes Mellitus (DM) on treatment outcomes of patients with pulmonary tuberculosis (PTB) in Yerevan, Armenia after adjusting for confounding factors.

Methods: The research team used a retrospective cohort study design to address the research question of interest. The study population included all adult patients registered in Yerevan TB care outpatient facilities whose treatment outcomes were recorded in the database of the Armenian National Tuberculosis Control Center (ANTCC) for the period 1 January 2013 to 31 December 2014. The study had two comparison groups: TB patients who had DM were in the exposed group and those without DM were in the non-exposed group. The electronic database of the ANTCC was reviewed to obtain the list of all eligible participants and necessary variables. Information on comorbidities, height and weight of patients were extracted from medical records of patients in eight outpatient TB facilities and the prison hospital in Yerevan. The dependent variable of the study was the TB treatment outcome defined by the World Health Organization: successful treatment, failure, died, and lost to follow up. The main independent variable of interest was the presence or absence of diabetes. The difference of baseline characteristics between two groups were compared using χ^2 and independent samples *t*-test. Multivariable logistic regressions was conducted to construct the final model and test the associations.

Results: In the sample of 621 TB patients 36 had diabetes (5.8%); 2.2 times higher than the prevalence of DM in general population in Armenia ($P < 0.001$). The odds of failure treatment outcome was much higher among TB patients with DM (OR=9.49; 95%CI 2.65–33.98, $P = 0.001$) compared to TB patients without DM after adjusting for confounding.

Conclusions: The study found that having DM negatively influenced the TB treatment outcomes. TB patients with DM were more likely to fail their TB treatment than TB patients without DM. Mechanisms should be developed to enforce the Ministry of Health guidelines for screening DM patients for TB and TB patients for DM. TB care specialists should be encouraged to more attentively manage the TB treatment process among patients with DM.

PD-866-28 Is diabetes mellitus a risk factor for relapse among tuberculosis patients on directly observed treatment?

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Background: Diabetes Mellitus (DM) is the known risk factor for tuberculosis (TB). There is a growing awareness on a global scale on the possible relationship between TB and DM. The aim of this study was to see whether there was any association between diabetes mellitus and tuberculosis relapse among patients who were taking DOTS.

Methodology: A case-control study was conducted among the cohort of pulmonary TB that was notified during 2012-2013 and had completed anti-TB treatment under Revised National Tuberculosis Control Programme (RNTCP), Chandigarh. One hundred and twenty relapse cases who were enrolled for TB treatment under RNTCP in the year 2012-13 in Chandigarh. For each relapse case, one control was selected from the same study cohort. DM status was ascertained by reviewing the medical records and by testing for HbA1C levels in the blood samples. The proportion of Diabetes Mellitus patients among cases and controls were compared and adjusted OR was calculated using conditional LR after adjusting for confounders.

Results: Presence of DM during anti-TB treatment was 22.5% and 25% among cases and controls, respectively. After adjusting for other potential confounders, it was found that DM was not significantly associated with increased risk of TB relapse (adjusted odds ratio: 0.86, 95%CI 0.45-1.65). The place of residence (OR: 2.04 95%CI 1.09-3.70) was significantly associated with TB relapse apart from number of missed doses the patient had during their anti-TB treatment (OR: 4.54 95%CI 1.19-16.67).

Conclusion: More emphasis should be given on strict adherence to the treatment for preventing relapse. TB programs should consider educating and motivating of patients as well as rigorous glucose control in TB patients. The follow up of the successfully treated tuberculosis cases should be done for 3-4 years so as to rule out any likelihood of relapse.

PD-867-28 Diabetes in tuberculosis patients in Iraq: prevalence and impact on treatment

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Background: Diabetes and Tuberculosis (TB) epidemics coexist. Diabetes affects the course of TB disease by increasing its incidence and affecting its treatment outcome. This study aimed at studying the prevalence of diabetes in TB patients in Iraq and the impact of diabetes on TB treatment outcome.

Methods: Patients attended 54 randomly selected basic TB management units out of 128 units in all Iraqi provinces. Recruitment continued 12 months from November 2013 to October 2014. Data inquired for both TB and diabetes diseases, and patients then followed till treatment completed. The χ^2 test for independence was used for studying associations and multinomial logistic regression used to assess the impact of diabetes on TB treatment outcome (the dependent variable was treatment outcome and the independent variable was diabetes). Ethical clearance and patient consent obtained before data collection.

Results: This study recruited 1157 PTB patients who were sputum positive for AFB. Age varied from four to 88 years. Males constituted 638 (55%) of the sample. Diabetes was prevalent in 282 patients [24.4 (95%CI 22.0-27.0)]. Diabetic TB patients were significantly older (51.6 ± 13.4 y) than non-diabetic TB patients (36.1 ± 17.4 y) ($P < 0.05$). Among diabetic patients, the prevalence of diabetic increase with the increase in age that affected around halve (159/315) the TB patients aged 45-64 years. There was no significant association between sex and diabetes in TB patients ($P > 0.05$). Simple cross tabulation revealed no significant association between diabetes and TB treatment outcome but diabetes was prevalent among TB patients ended with death (14/37; 38%) and further analysis with logistic regression revealed that diabetes is a significant risk factor for death in TB patients [OR=2.0 (95%CI 1.0-4.1)] but not for other undesirable outcomes.

Conclusions: Diabetes has a considerable prevalence in Iraqi TB patients and doubles the probability of their death.

PD-868-28 Clinical manifestations of tuberculosis in patients with pulmonary tuberculosis (TB) and TB combined with different types of diabetes

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Background: The aim of our study was to a comparison of the clinical manifestations tuberculosis (TB) in patients with TB and TB combined with different types of diabetes mellitus (DM).

Methods: We studied 245 patients who were divided into 3 groups. The first group included 45 patients with pulmonary TB combined with DM I type, the second, 69 patients with pulmonary TB combined with DM type II, and the third, 130 patients with pulmonary TB without DM.

Results: Comparative analysis of the clinical characteristics of patients examined showed that the sex composition of the group did not differ. In all three groups dominated by men (53.3%, 50.7 and 53.4%, respectively). Women accounted for 46.7%, 49.3 \pm % and 46.6%,

respectively. The age of patients in the first group ranged from 19-59 years, the second 21-76 years, and the third 18-74 years. It was found that tuberculomas in patients with DM type I was diagnosed in 33.3% of patients; in 31.9% with type II diabetes, and in patients without diabetes only in 8.4% (respectively $P_{1-3} < 0.008$; $P_{2-3} < 0.01$). On the contrary, infiltrative pulmonary tuberculosis was diagnosed in 20.0%, 29.0% and 44.3% patients respectively ($P_{1-3} < 0.05$). Furthermore, the number of patients with caseous pneumonia in patients with pulmonary tuberculosis combined with diabetes type 1 were higher (respectively 11.1%, 4.4% and 1.5%, $P_{1-3} < 0.01$). *M. tuberculosis* was detected in sputum of 68.9% of patients with DM type I, in 72.5% of patients with DM type II and in 58.8% of patients without DM ($P_{2-3} < 0.05$). Cavities in the lung were detected in 93.3% of patients with DM type I, in 94.2% of patients with DM type II and in 76.3% of patients without DM ($P_{1-3} < 0.01$ and $P_{2-3} < 0.01$).

Conclusions: Clinical manifestations of pulmonary tuberculosis in patients with combined diabetes have their own characteristics. In these patients, in contrast to patients with pulmonary tuberculosis was significantly more diagnosed tuberculom with destruction. In addition, the number of *M. tuberculosis* positive patients was higher in this category of patients that, probably due to the characteristics of tuberculoma flow in these patients.

PD-869-28 Indonesia's tuberculosis-diabetes registry: comparison of sputum smear and culture results for tuberculosis diagnosis in patients with and without diabetes comorbidity

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Background: With an estimated 1 million new cases in 2014, almost 2.5 fold increase compared to 2013, tuberculosis (TB) in Indonesia remains as serious problem. This number may escalate in the future due to the increasing people affected with essential comorbidity of TB such as Diabetes (DM) that will lead to higher number of people seeking TB care. In order to provide basic evidence of TB-DM burden in Indonesia, the National Institute of Health Research and Development (NIHRD), Ministry of Health of Indonesia created the TB-DM Registry in 2014.

Methods: TB-DM Registry is one of disease registries conducted by NIHRD. Seven hospitals in level of province were actively participated in this registry by collecting the data of adult with pulmonary TB patients in the hospital using online data form provided in INA Registry website. This article analyzed data from TB-DM Registry to assess the result of sputum smear and culture results on TB patients with DM comorbidity and to compare the results against patients with no comorbidity.

Results: Sputum smear results were available from 1136 TB patients and 534 of them also have culture results. About 16% (178) of these patients were TB-DM patients and the rest of them are without DM status. There is statistically significant difference on positive smear result between two groups ($P < 0.001$). The culture test results also showed statistically significant difference ($P = 0.025$). The complete results are shown in the Table.

Conclusions: This study identified the different results of sputum smear and culture tests between TB patients with and without DM. These findings may indicate the necessary to have different approach on management of those two groups.

Table A) Comparison of smear results TB DM and TB No DM

	No-DM comorbidity (n = 958)	DM comorbidity (n = 178)	P value
Sputum smear			
Negative	335 (34.97%)	26 (14.61%)	0.000
Positive	623 (65.03%)	152 (85.39%)	

B) Comparison of culture results TB DM and TB No DM

	No-DM comorbidity (n = 431)	DM comorbidity (n = 103)	P value
Culture			
Negative	122 (28.31%)	18 (17.48%)	0.025
Positive	309 (71.69%)	85 (82.52%)	

PD-870-28 Impact of poorly controlled diabetes and adverse drug reactions on treatment outcome in patients receiving directly observed treatment for TB: a prospective study

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Background: Tuberculosis and diabetes mellitus are two public health problems which not only often coexist but have serious implications on each other. Poorly controlled DM patients is on higher risk, as elevated HbA1c concentration of > 7 mmol/mol is associated with decreased phagocytic activity and T-cell functioning results in impaired cell mediated immunity. The present study focuses on the impact of uncontrolled diabetes and adverse drug reactions on the treatment outcome, compared with controlled diabetes on TB patients under DOTS therapy.

Methods: Eligible TB patients were subjected to blood glucose screening under fasting condition at treatment initiation time. Patient found diabetic during screening, underwent HbA1c estimation for glycemic index determination at the end of I.P and C.P. Patients having average HbA1c ≥ 7 mmol/mol were considered as uncontrolled diabetic while those of < 7 mmol/mol were controlled diabetic. The clinical presentation and treatment outcomes were compared between controlled diabetic and un-controlled diabetic TB patients. The

ADRs were recorded in the suspected adverse drug reporting form i.e., the voluntary reporting of adverse drug reactions by healthcare professionals. Odds ratio was calculated by logistic regression analysis for sputum conversion, treatment outcome and ADR incidence due to anti-TB drugs.

Results: Out of total 316 patients, prevalence of DM was found 15.8% (50/316), in which 19.4% and 9.6% were PTB and EPTB patients respectively. It was observed that 33 (66.0%) and 17 (34.0%) patients with controlled and un-controlled diabetic patients respectively. In PTB patients, 8.4% and 23.1% patients were finished with unsuccessful outcome at the end of treatment in controlled and uncontrolled diabetes respectively. More patients remain sputum positive at the end of I.P in uncontrolled diabetic patients. ADRs were recorded in total of 92% diabetic patients.

Conclusion: Poorly controlled diabetes has poor treatment outcome and cause more ADR incidence among TB patients. Screening for DM is recommended in TB patients with all age group could improve the treatment outcome and diagnosis and early management of DM complications.

27. MDR drugs: access, supply and cost

PD-871-28 Too little, too late: new anti-tuberculosis drugs for patients with complex drug-resistant tuberculosis in Mumbai

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Background: Mumbai has a large burden of complex patterns of drug-resistant tuberculosis (DR-TB). Designing an effective treatment regimen with four working anti-TB drugs is nearly impossible for several patients. Two new drugs—bedaquiline (BDQ) and delamanid (DLM)—have renewed hope for improving individual outcomes and stopping DR-TB transmission. Médecins Sans Frontières (MSF) has been treating DR-TB-HIV in Mumbai since 2006, and introduced BDQ and DLM through compassionate use (CU) in 2013 and 2015 respectively. The aim of this study is to describe programmatic experiences with BDQ/DLM in the treatment of complex DR-TB patients.

Methods: This was a retrospective cohort study among DR-TB patients who received BDQ/DLM between February 2013 and December 2015.

Results: Of 223 DR-TB patients, 23 were eligible (11-BDQ; 12-DLM). Sixteen patients were female; aged 17-38 years and two HIV-co-infected (BDQ-group). Five patients had pre-extensively and 18 extensively DR-TB. Two patients had no previous history of exposure to second line anti-TB drugs. All 11 patients started BDQ treatment but 9/12 started on DLM; two patients died before treatment initiation and regimen for one patient

could not be designed (single working drug). BDQ/DLM was added to backbone-regimen in baseline culture-positive/negative DR-TB patients (BDQ-group: 9 culture-negative, 2 culture-positive; DLM-group: 3 culture-negative, 6 culture-positive). 3/11 patients in BDQ and 10/12 in DLM-group had < 2 likely-working drugs (either susceptible in DST-results and/or < 3 months of exposure) in their regimen. Imipenem was added to all patients in DLM-group. By January 2016, 11/23 patients had sustained culture-conversion to negative. Serious adverse-events were recorded in two patients (one in each BDQ/DLM-group); none had to permanently stop treatment. Two deaths (one in each BDQ/DLM-group) were reported; cause of death could not be ascertained.

Conclusions: A large proportion of patients eligible for CU of new drugs have exhausted most likely working drugs. Adding BDQ or DLM alone to a weak backbone regimen bears a high risk of adverse treatment-outcomes and resistance amplification to newer drugs. There is an urgent need for combination treatment with potent drugs like BDQ-DLM. Rather than adopting a 'too little, too late' approach in settings with complex TB resistance patterns, we should treat DR-TB promptly and proactively.

PD-872-28 Drug use reviews: an approach for ensuring the rational use of anti-tuberculosis and antiretroviral medicines in Ukraine

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Background and challenges to implementation: The prevalence and characteristics of inappropriate TB regimens have been reported in the literature (Langendam, et. al.). From 2012 to 2015 the US Agency for International Development (USAID) funded Systems for Improved Access to Pharmaceuticals and Services (SIAPS) Program provided technical assistance to the Ministry of Health of Ukraine (MOH) and the National TB Program (NTBP) in the area of rational drug use (RDU). Assistance included introducing Drug Use Reviews (DURs), a practical strategy to ensure the appropriate use of medicines. The first review assessed the level of physicians' adherence to MDR-TB treatment standards.

Intervention or response: Using a retrospective medical record review process we screened charts from a cohort of 68 MDR-TB patients who received inpatient treatment from January to August 2014. We were able to evaluate data from 40 patients that were then subdivided into four cohorts according to treatment regimen. Trained data collectors captured data using a collection tool (individual registration form). Data included detailed information about dosage, administration frequency, laboratory tests, and adverse events. The data was compared to Ukrainian treatment standards.

Results and lessons learnt: Lack of adherence to treatment standards while caring for MDR-TB patients is the main finding. Inadequate frequency of administration and unjustified substitution of TB medicines, insufficient adverse event management, and a deficiency of laboratory resources were also observed as limitations for optimal treatment results. TB DURs are not a day-to-day practice in Ukraine, hindering benefits of continuous of treatment monitoring. In response, efforts have been undertaken set up the Drug and Therapeutics Committee (DTC) and to develop other tools enabling continuous drug use monitoring in TB facilities. DUR methodology has been adopted by the National HIV Program. Two AIDS Centers in Ukraine started antiretroviral DURs 2015.

Conclusions and key recommendations: In 2016 MOH of Ukraine initiated development of the National Drug Policy (NDP). Through an initiative of the NDP Working Group and SIAPS, regulations establishing DTCs in healthcare facilities were incorporated into the NDP. The first TB DUR opens doors for institutionalization of the approaches and methodologies provided by SIAPS across all public health programs.

PD-873-28 Removing one of the major barriers to accessing bedaquiline and delamanid, life-saving treatments for MDR-TB patients

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Background and challenges to implementation: For the first time in more than 40 years, two new compounds, namely bedaquiline (BDQ) and delamanid (DLM), have been conditionally approved for the treatment of multidrug-resistant tuberculosis (MDR-TB) and extensively drug-resistant TB (XDR-TB). Since then, the respective registration of BDQ and DLM has occurred only in a limited number of countries. In a recent survey conducted by the Stop TB Partnership and Médecins Sans Frontières, the lack of registration of these two drugs was identified as the main barrier for their use in MDR-TB treatments. The registration of BDQ and DLM by national regulatory authorities and their inclusion in the National Essential Medicine List (EML) are essential steps for scaling up their introduction.

Intervention or response: A detailed web-based questionnaire was developed to survey the situation in the registration process and the inclusion of BDQ and DLM in the EML within the 30 WHO identified high MDR-TB burden countries. The questionnaire was tested for validity and reliability. Content validation was followed by test-retest validation and the questionnaire was sent to key national representatives.

Results and lessons learnt: Main obstacles to expedited registration and EML inclusion of BDQ and DLM in countries were identified from the detailed information obtained from the surveyed countries, manufacturers and key stakeholders. Lessons learned collected from coun-

tries where the drugs have been successfully registered and/or included in the national EML and proposals on how to adapt these positive examples to similar contexts will be presented.

Conclusions and key recommendations: The results of our survey enable all partners involved in the registration process to have a clear overview of the registration status of BDQ and DLM in 30 high MDR-TB burden countries, thus supporting them to act accordingly to accelerate the registration process. Lessons learnt from countries where the drugs have been successfully registered provide further inputs that can be exploited to improve access to BDQ and DLM.

PD-874-28 Country perceptions for implementation of new multidrug-resistant TB medicines

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Setting: An estimated 480 000 new multi-drug resistant TB (MDR-TB) cases and 210 000 deaths were reported in 2013. The current treatment for drug resistant TB is long, complex and associated with severe and life threatening side effects with successful treatment outcomes of approximately 50%. There have recently been two new drugs registered for use in multi-drug resistant TB (MDR-TB), bedaquiline and delamanid with WHO interim guidance on their use. These medicines offer great potential for improving MDR-TB treatment but the scale up in their use has been slow.

Objective: To learn countries points of view, barriers, intention to incorporate the new medicines into treatment regimens and policies, Stop TB Partnership collaborated with Médecins Sans Frontières (MSF) to conduct a survey among national TB programmes of MDR-TB high-burden countries. The survey was sent out to 27 countries on March/2015 and 25 countries had responded by June 2015 when the survey was closed.

Results: Results show that 24 countries are aware of the new medicines but only 28% have registered bedaquiline and 12% delamanid for use. With regards to a framework for Compassionate Use or other mechanism allowing pre-approval access 68% of the countries have access to bedaquiline though this and 56 % for delamanid. Most popular reasons cited by countries for limited or non-usage of the medicines are (i) the medicines are not registered in the country (ii) economic barriers i.e. the cost of the medicine and/or companion medicines among others, (iii) concerns about the side effects, (iv) limited knowledge of the drugs and (v) practitioners not trained in their administration.

Conclusion: Question on whether countries would recommend the use of the new medicines, responses show that most countries are comfortable on using the medicines and strongly recommend their use in the treatment of MDR-TB.

PD-875-28 Implementation of a bedaquiline access programme for the treatment of drug-resistant tuberculosis in the Western Cape, South Africa

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Background and challenges to implementation: In 2011, the Western Cape Province operationalized decentralized services for the treatment of Drug Resistant Tuberculosis (DR-TB). These services were implemented at Primary Health Care (PHC) sites, which are nurse-driven. Despite decentralization, the DR-TB defaulter rate remained above 30% due to side-effects and intolerability of DR-TB drugs. In October 2014, the Medicines Control Council approved the use of bedaquiline for the treatment of selected DR-TB patients. Bedaquiline had a more favourable side-effect profile and was well tolerated in trials. Only two sites were approved for initiation of treatment with this new drug in the Western Cape.

Intervention or response: A clinical advisory committee was established, with the role of providing clinical oversight for management of patients on bedaquiline. The committee assisted with the development of training material and mentoring of clinicians. Training was offered in both metro and rural districts. It therefore became feasible to discharge stable patients from the approved sites back into the community, to continue receiving their medication and monitoring at Primary Health Clinic (PHC) sites. Due to the new demand for treatment with bedaquiline, it was necessary to allow suitably trained and supervised clinicians at PHCs to initiate bedaquiline in MDR-TB patients requiring drug substitution, effectively decentralizing the treatment.

Results and lessons learnt: Electrocardiogram (ECG) monitoring was not available at the PHC sites. Standard Operating Procedures for ECG monitoring at Community District Centers (CDCs) was therefore developed in order to fast track patients through the system. Buy-in from staff and training around interpretation of ECGs became important. Unfortunately, 12 patients died while on bedaquiline. Many of these patients had co-morbidities, with insufficient clinical evidence implicating bedaquiline as the cause of death, resulting in requests for medico-legal autopsies being declined. The advisory committee have engaged with Forensic Pathology Services on the matter.

Conclusions and key recommendations: Since the implementation of the bedaquiline access programme in April 2015, 372 patients have been initiated on treatment. Decentralization of DR-TB treatment prevents unnecessary hospitalization for extensive periods, and enables clinicians to prioritise hospital beds for patients who are more in need of specialised care.

PD-876-28 Achievements and challenges in accessing new drugs for drug-resistant TB patients managed in primary care settings in Khayelitsha, South Africa

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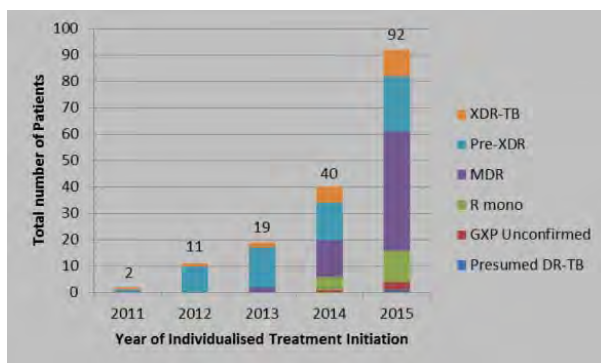
Background/challenges to implementation: Approximately 200 patients with rifampicin-resistant tuberculosis (RR-TB) are managed by primary health care (PHC) clinicians each year within a decentralised model of care in Khayelitsha, South Africa. Complicated cases or those with second-line drug resistance usually have limited access to new TB drugs (linezolid, bedaquiline, delamanid) outside of specialist hospitals or clinical trials.

Intervention: Through strong advocacy and collaboration between local partners, department of health and pharmaceutical agencies, Médecins Sans Frontières (MSF) secured access to linezolid in 2011, and Khayelitsha became a designated site for the national clinical access programme for bedaquiline in 2012. MSF sourced delamanid through compassionate use in 2015. Additional staff training, clinician support, pharmacovigilance, monitoring and evaluation, patient support and community awareness was provided for introduction of these new drugs within the decentralised model of care.

Results: Since July 2011, 164 (14.9%) out of 1096 treated RR-TB patients initiated individualised treatment regimens (83 [50.6%]) in local PHC facilities within Khayelitsha) including one or all of linezolid, bedaquiline and delamanid (see Figure). Challenges to access included: high cost of drugs, particularly linezolid; delayed registration of new drugs in South Africa; and time to approval of individual cases reviewed by various clinical committees. Among the 100 patients receiving bedaquiline, median time to initiation of bedaquiline has decreased over time (2.6 months in 2013 to 1.8 months in 2015) thanks to the successful wider rollout of the national access programme for new drugs in South Africa.

Conclusions: Strong advocacy focused on widening patient eligibility criteria, new drug registration and price reduction of existing drugs along with collaboration between local, national and international partners can improve access to new TB drugs. Decentralisation of services to PHC level allows clinically stable patients to be managed with new TB drugs outside of hospital once adequate protocols are implemented.

Figure Number of DR-TB patients receiving individualised regimens



PD-877-28 Strengthening quality assurance systems of pharmaceutical manufacturers to ensure availability of affordable TB medicines on the global market

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Background: The use of poor quality TB medicines prevents the successful treatment of TB and contributes to development of drug-resistance. To ensure use of good quality medicines, the Global Drug Facility (GDF), Global Fund, and other international and nongovernmental organizations mandate that only medicines prequalified by WHO, or approved by stringent regulatory authorities (SRAs) are suitable for procurement. The US Agency for International Development (USAID) funded Promoting the Quality of Medicines (PQM) program provides technical assistance to pharmaceutical manufacturers to ensure that TB medicines meeting international quality standards and of competitive price are available to the public market.

Intervention: PQM works with global partners to identify manufacturers of critical TB medicines to provide technical assistance to strengthen their quality assurance systems and achieve WHO prequalification and/or approval in stringent regulatory markets. The technical assistance encompasses all areas of pharmaceutical quality assurance including product development, technology transfer, scale-up, dossier compilation and submission, and Good Manufacturing Practices (cGMP). PQM assistance continues well after the product dossier is submitted to the regulatory body, to address questions on dossier and inspection, until the product receives final approval.

Results: As a result of PQM technical assistance, 11 TB medicines achieved WHO prequalification or SRA approval between 2011-2016. This intervention has increased the availability of quality-assured TB medicines on the global market. With PQM support, the first quality-assured sources for Capreomycin, Kanamycin and Levofloxacin active pharmaceutical ingredients

(APIs) received WHO Prequalification and/or USA Food and Drug Agency approval. APIs from these sources will help alleviate concerns about vertical integration and potentially diversify the sources of finished pharmaceutical product manufacturers. In addition, increasing the pool of WHO prequalified or SRA approved medicines contributed to the decrease in medicines prices. After the first generic Capreomycin FPP achieved WHO prequalification, the price per unit decreased on average by more than 50%.

Conclusion: PQM assistance to TB manufacturers has a significant impact in shaping the global market and has contributed to increasing the availability of quality-assured TB medicines at competitive prices. This has translated into savings for donor and public funds for the procurement of TB medicines.

PD-878-28 Cost analysis of models of care during the intensive phase of multidrug-resistant tuberculosis treatment at St Peter's Hospital, Ethiopia

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Background: Models of centralized in-patient care in high TB burden countries where there are insufficient bed capacity result in newly diagnosed Multi-Drug Resistant Tuberculosis (MDR-TB) patients placed on long waiting lists for an in-patient bed. Recently, an alternative, community based treatment or ambulatory models have been developed and adopted in various countries. Objective This study was conducted to assess and compare the effectiveness and cost of inpatient and ambulatory models of care in treating MDR-TB during the intensive phase at St. Peter's TB specialized hospital Ethiopia.

Methods: Retrospective cross sectional study involving 204 patients (109 inpatient and 95 ambulatory) who were on continuation phase of MDR-TB treatment from February 18 to 20 April 2015 was conducted using a standardized questionnaire. The effectiveness measure was the number of patient who completed the intensive phase and moved into the continuation phase within the prescribed period. Cost data was extracted from hospital budget documents.

Results: The total cost per hospitalized patient during the intensive phase of treatment was 1.2 higher than the ambulatory model and has significant difference ($P < 0.023$). This accounts 4083.4 USD for the hospitalized (572.83 USD patient cost). The DALY averted by ambulatory model was 319.65 USD and 412.9 USD for hospitalized. The DALY saved by the ambulatory model was 1 month and ICER was 932.5 USD per year.

Conclusion: In general, the results suggest that ambulatory model cost less than the inpatient model in treating MDR-TB patients during the intensive phase.

PD-879-28 No severe hearing loss detected with pure tone audiometry in patients treated with short-course MDR-TB treatment in Niger

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Background: The majority of published studies on ototoxicity in patients treated with second line drugs are based on clinical monitoring. However pure tone audiometry (PTA) reveals mild ototoxicity even in patients without any hearing complaints. Our goal was to analyse the hearing loss with PTA in multidrug-resistant tuberculosis (MDR-TB) cases treated with short-course regimen.

Methods: This was a retrospective cohort study. Patients with confirmed MDR-TB not previously exposed to second line drugs were treated with 9 to 11 months regimen with an intensive phase containing kanamycin from 4 to 6 months. They were enrolled between January 2014 and October 2015. PTA was performed at the start (M0) and at month 4 (M4). Hearing losses were graded according to the International Bureau of Audiophonology. The degrees were: D0: normal or subnormal (< 20 dB); D1: mild (21-40 dB); D2: moderate (41-70 dB); D3: severe (71-90 dB); D4: profound; permanently disabling (>90 dB).

Results: A total of 67 patients were enrolled, 57 (85.1%) were males and the mean \pm SD age was 35 ± 8.3 years. The mean BMI was 18.2 ± 2.4 kg/m². There were 3 HIV positive tests (4.5%). The mean duration of the intensive phase was 4.2 ± 0.3 months. Forty-three (64.2%) patients previously took 2 months of streptomycin and 18 (26.9%) had a mild (D1 15; 22.4%) to moderate (D2 3; 4.5%) hearing loss at baseline. No patient had a severe degree of ototoxicity. After 4 months of kanamycin, 42 (62.7%) patients had mild (30; 71.4%) to moderate (12; 17.9%) hearing loss with significant difference to baseline ($P < 0.025$; OR 2.82, CI95% 1.4-5.68). We found no cases with severe or profound degrees of ototoxicity. There was no difference in hearing loss (normal vs. abnormal audiometry) between M0 and M4 statistically associated to BMI, previous use of streptomycin and abnormal audiometry at baseline.

Conclusion: Early detection of ototoxicity is important in patients treated with aminoglycosides in order to replace or to reduce the dose of the offending drug. The PTA revealed mild ototoxicity not reported in clinical based monitoring studies. No cases of severe hearing loss were recorded with the 9-month regimen.

PD-880-28 Minimum inhibitory concentration testing can improve multidrug-resistant tuberculosis regimen choice in Bangladesh

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Background: Minimum inhibitory concentration (MIC) testing has excellent correlation with conventional drug susceptibility testing (DST). Yet susceptible MICs near the critical concentration for determining resistance may place a patient at risk of poor outcome, particularly when treated with empiric regimens. In Bangladesh, both the WHO Category IV and other modified regimens (eg. Bangladesh) are used, allowing comparative assessment. **Methods:** Adults were surveilled throughout Bangladesh during 2011-2015 at multidrug-resistant (MDR)-TB treatment initiation. *M. tuberculosis* isolates had MIC testing by the Sensititre MYCOTB plate for 12 anti-TB drugs, and those with rifampin resistance were included. MIC values were compared within medication class and against the patient's MDR-TB drug regimen.

Results: Eighty-eight patients with rifampin-resistant *M. tuberculosis* were analyzed, with mean age 31 years (± 11) and 40 (45%) were female. Among all isolates, the isoniazid median MIC was 1.0 μ g/ml (interquartile range 0.5-4.0 μ g/ml) with 13 (15%) at or below 0.5 μ g/ml (concentration where high-dose isoniazid may be effective) compared to rifabutin with median 1.0 μ g/ml (0.5-4.0 μ g/ml) where 31 (35%) isolates were fully susceptible ($P = 0.03$). Non-S531L mutations in *rpoB* were more common among isolates with lower rifabutin MIC. The ofloxacin median MIC was 2.0 μ g/ml (1.0-8.0 μ g/ml) with 52 (58%) at or within one dilution lower than the critical concentration. Excluding those with frank ofloxacin resistance (MIC >2.0 μ g/ml), in patients with known treatment outcome, 21 had an ofloxacin MIC of 2.0 μ g/ml (only one with *gyrA* mutation) and 6 (29%) suffered death or lack of 6 month culture conversion, compared to 2 of 24 (8%) with MICs of 1.0 μ g/ml or less (none with *gyrA* mutation) ($P = 0.08$). Furthermore, among 44 patients receiving a modified regimen, 9 (20%) had MICs that suggested benefit from high-dose isoniazid and 28 (63%) from later generation or higher dose fluoroquinolone.

Conclusions: MIC testing would alter MDR-TB regimen choice in Bangladesh particularly in the use of later generation and/or higher dose fluoroquinolones and high-dose isoniazid. Rifabutin susceptibility appears common, hence rifabutin DST and use of the drug should be considered in this setting.

28. 'Getting better': service delivery reforms to enhance patient centred-care

PD-881-28 Integrating tuberculosis care in designated hospitals in Zhejiang Province, China: implications for service delivery

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Background: There is on-going debate regarding if and how integrated service delivery might affect quality of care for infectious diseases traditionally delivered through vertical programmes. In China, tuberculosis (TB) care has recently been integrated into 'designated' public hospitals at the county level. This initiative is built on the assumption that hospitals have stronger technical capacity, and can provide better quality of care. This study uses prescribing practices among hospital-based TB clinicians as a lens to explore the implications of integrated service delivery for provider behavior and quality of care.

Methods: This study was conducted in two separate TB clinics set up within designated hospitals, funded either through local government, or the hospital. We reviewed 340 medical records of uncomplicated TB patients and conducted 43 in-depth interviews with health officials, TB/hospital managers, clinicians, radiologists, laboratory staff and nurses.

Results: Standardized care for uncomplicated TB, including outpatient-based diagnostic services and TB drugs, is free. In both hospitals, however, non-standardised prescription of drugs and interventions for uncomplicated TB was common, with no consistent patterns for the two hospitals. Overall, 77%, 53%, 51% and 5% of the patients were prescribed with computerised tomography (CT) scan, liver protection drugs, immune improvement drugs and hospitalizations respectively. Non-standardised prescribing practices could be linked to professional status of the TB clinicians who see themselves as distinct from public health doctors traditionally responsible for TB services. Hospital-based integrated TB care is highly medicalised: doctors justified, for example, the use of liver drugs to prevent side effects of the TB drugs; CT scans to improve diagnostic capacity; and hospitalizations to reduce transmission of TB.

Discussion/conclusion: Clinicians striving to maintain professional status in the face of integrating a public health problem within a hospital setting has led to over-medicalised and to some extent, costly, prescriptions for TB patients. This trend may also be seen as a self-protective mechanism in the context of deteriorating doctor-patient relationships in China. Our study indicates that integrating TB care in Chinese hospitals may have an adverse effect on quality of TB care, unless public

health values are better incorporated with medical doctors' routine practices.

PD-882-28 Improving ART uptake and treatment outcomes among TB-HIV co-infected patients by implementing a one stop model of care in Kampala, Uganda

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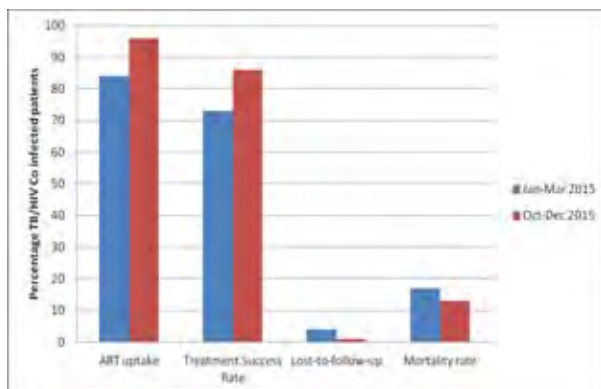
Background and challenges to implementation: About 30% of TB-HIV co-infected patients in Uganda did not promptly receive antiretroviral therapy (ART) during 2013 due to gaps in coordination of TB and HIV care. The Ministry of Health National TB Programme adapted the one-stop shop model of integrated TB-HIV care and implemented it in Kampala with support from the USAID-funded TRACK TB project. We demonstrate the results of implementing the one-stop care model at selected health facilities in Kampala.

Intervention or response: Care teams at 13 health facilities were trained using mentorship and quality improvement coaching approaches to implement the patient centered one-stop model for TB-HIV service delivery at the TB care point. Care teams synchronized client consultations, counseling, sample collection, drug dispensing and appointment giving; reorganized their client flow; harmonized the movement and storage of their TB-HIV facility records and regularly reviewed their performance on TB treatment outcomes.

Results and lessons learnt: Eleven out of the 13 health facilities (85%) that had previously provided TB and HIV care at separate care points successfully established the one-stop TB-HIV care point. The patient care outcomes of the intervention are illustrated in the Figure.

Conclusions and key recommendations: Integration of HIV care and treatment in TB services improves ART uptake, retention of TB-HIV co-infected patients in care, and TB treatment outcomes, and reduces mortality. The model should be adopted in for high burden settings with low TB-HIV performance indicators to improve the quality of patient care and treatment outcomes.

Figure Outcomes of TB-HIV patients receiving care through a one-stop model at 11 health facilities



PD-883-28 The need to restructure TB hospitals in the Kyrgyz Republic

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Background and challenges to implementation: The TB control policy in the Kyrgyz Republic has been brought in accordance with the modern international standards. TB guidelines were approved by the Ministry of Health based on the outpatient treatment priority. It reduces demand in TB beds. The Ministry of Health created working group to conduct assessment of TB hospitals performance and develop recommendations on restructuring TB hospitals network in the country.

Intervention or response: All of 24 TB hospitals (2605 beds) were included in the analysis. Data on the hospital treated cases for 2014 from the Mandatory Health Insurance Fund Database, reporting data on the hospital performance (Form 14) were used for analysis. Additionally, an assessment of patients' room spaces, availability of service rooms and ventilation was undertaken for compliance with existing sanitary standards. The analysis addressed validity of reasons for hospitalizations, length of stay, bed occupancy rate, TB doctors' workload and compliance with infection control requirements.

Results and lessons learnt: 13 491 cases were treated in TB hospitals in 2014. Among them, 1952 (14%) cases were not TB cases and 5276 (39%) were extra-pulmonary TB, or smear-negative pulmonary TB. Totally, 53% cases were cases with unjustified hospitalizations. Average length of stay varied from 40 to 152 days, bed occupancy rate from 41 to 127% and average workload per one TB doctor was 6.8 ± 2.8 patients a month. Square of 5.8 ± 2.9 m² per one bed; availability of only one service room per TB unit; absence of mechanical ventilation and other engineering instruments of infection control explain high risk for hospital-acquired TB & MDR-TB infection.

Conclusions and key recommendations: Efficiency of TB hospitals in the country is low, their current number is exaggerated and expenses are unjustified. Recommendations on the optimization and restructuring of TB hospitals are included in the National strategic document entitled Road map on further development of TB care in the Kyrgyz Republic. Money saved is planned to be redirected to the improvement of medications supply, infrastructure of remaining TB hospitals as well as quality improvement of TB services at primary health-care level.

PD-884-28 Cost-effectiveness of public-private mix models for enhancing case detection of tuberculosis in Viet Nam

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Background and challenges to implementation: As the majority of patients with presumed tuberculosis (PWPTB) in Viet Nam often seek care at pharmacies, private clinics and general hospitals first, public-private mix (PPM) is an important strategy to increase case detection. With GFATM funding, PATH implemented a comprehensive PPM program in high-burden provinces of Hanoi, Ho Chi Minh City, Binh Dinh and Ba Ria-Vung Tau during 2011-2015.

Intervention or response: The program mobilized 1,894 health facilities (817 private clinics/hospitals, 1001 pharmacies and 76 public hospitals not formally linked to the national tuberculosis program (NTP) in 28 districts of four provinces to identify and refer PWPTB to TB facilities for diagnosis (referral model). A further model was also implemented to engage 18 public hospitals in the diagnosis of TB (diagnosis model). An evaluation included analysis of monitoring data, review of NTP data, and key informant interviews to assess outcomes and impact of PPM activities on case detection. A cost analysis of investment and recurrent expenditures (excluding diagnosis cost) was also undertaken to compare the respective TB case detection unit cost of the diagnosis and referral models.

Results and lessons learnt: Among 1894 facilities in the referral model, 733 (39%) referred 24 290 PWSTB to TB facilities. Subsequently 17 209 (71%) of these referrals resulted in a TB diagnosis, and 3866 (22%) new TB cases were detected. Notably, the 18 facilities in the diagnosis model provided sputum smear tests for 19 148 PWPTB, and detected 4985 (26%) of new TB cases (all forms). The number of TB cases detected by PPM activities accounted for 16% (ranging 11-19%) of total cases detected in the participating provinces during the period 2012-2015. The cost analysis found the unit cost for detecting one new TB case in the diagnosis model (\$8.20) ten times lower than that of referral model (\$81.2). However, the referral model may detect TB cases earlier than diagnosis model.

Conclusions and key recommendations: PPM has proven an effective strategy to increase case detection. The Viet

Nam Ministry of Health endorsed and issued a policy (Circular 02/2013) to facilitate the nationwide scale up of PPM activities to enhance TB case detection.

PD-885-28 Social enterprise model for increased tuberculosis case detection in the private sector of Dhaka, Bangladesh

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Background: Tuberculosis (TB) control activities by the National TB Control Programs (NTPs) in high TB burden countries like Bangladesh should be supported with innovative and sustainable approach for a successful public private mix initiative. Private sector can be targeted to increase TB case detection as a step forward to identify the missed cases.

Intervention: Three Screening Centres (SCs) equipped with X-ray (CXR) and GeneXpert (GXP) systems were established in Dhaka under a social enterprise model (SEM) targeted to serve the presumptive TB cases identified at practice places of networked Private Physicians (PPs) in the private sector. A network of more than 1800 PPs (specialists and general practitioners) referring presumptive cases to SCs were established. From July, 2014 to February, 2016, the SCs received presumptive cases from the PPs, smear negative presumptive cases from DOTS and also self referred cases. The SCs offered CXR at a subsidized fee and free GXP using single spot sputum specimen. Identified TB cases were registered for treatment at NTP linked DOTS centres or under the referring PPs in the private sector following the NTP guideline.

Results and lessons learnt: During the period 19 230 CXRs were performed among the presumptive cases received from all sources at SCs. Sputum specimens were collected from 18 279 (95%) presumptive cases and were tested with GXP. A total of 3578 (18.6% of 19 230) pulmonary TB cases were identified; 2732 (15% of 18 279 GXP tested) cases were bacteriologically (B+) confirmed in GXP and 846 (4.4% of 19 230) were clinically diagnosed. Among the bacteriologically identified cases, 151 (5.5% of 2732) were rifampicin resistant cases. For initiation of treatment 71% patients got registered at DOTS and 9% at private sector with the referring PPs. The SEM detected 1053 additional B+ cases compared to baseline and contributed in detection of 28% of the total B+ cases identified in Dhaka.

Conclusions and key recommendations: Social enterprise model can be designed and scaled up for increasing TB case detection in the private sector. A large number of undiagnosed active TB cases can be identified using the model and thereby support NTPs in building stronger PPM linkages.

PD-886-28 The yield of TB screening in over 16 million out-patient department visitors in two regions of Ethiopia

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Background: Routine screening of outpatient department (OPD) visitors is one of the key tuberculosis (TB) case finding strategies. However, there is limited information on the yield and feasibility of this approach and whether a more targeted screening should be done is an unresolved issue. Our objective was to assess the yield and contribution of OPD screening to the overall case finding.

Intervention: Over the last four years, a USAID funded Help Ethiopia Improve Low TB performance (HEAL TB) collaborated with Oromia and Amhara regional health bureaus to improve case detection and treatment outcome. Training health care workers (HCWs) from health facilities and TB program managers, provision of TB screening and diagnostic algorithm and job aids were some of the supports given to enable the implementation of TB screening at outpatient department (OPD). In addition, the project provided laboratory supplies and issued technical and financial support for the regular health facility mentoring and supportive supervision. We computed the yield of TB case at OPDs from the routinely collected data.

Result: From October 2013 to September 2015, HCWs screened 16 236 064 OPD visitors in 1553 health facilities and detected 503 541 presumed TB cases (3.1%) of which they identified 96 512 TB cases, the yield being 0.6% from screened and 19.2% from presumptive TB cases. TB cases from OPD screening thus contributed to 77.5% of 124 537 all forms of TB cases notified over the same period in the two regions. The respective number need to screen (NNS) and number need to test (NNT) was 32.2 and 5.1 (Table).

Conclusion: OPD screening contributed to more than three-fourths of overall CNR in the two regions. The approach should be strengthened in high TB burden settings. Further analysis is needed to better understand the relative contributions of other case finding approaches.

Table The yield of TB screening at outpatient department visitors in two regions of Ethiopia

Total screened at OPD	16 236 064
Number (%) of presumptive TB cases identified	503 541 (3.1)
Number (%) TB cases detected	96 512 (0.6)
NNS	32.2
NNT	5.2

PD-887-28 Should smear-negative TB individuals with symptoms be actively followed up to identify missing cases in India? Study from Barmer, Rajasthan

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Background and challenges to implementation: Identification of sputum smear-negative pulmonary TB is challenging when compared with sputum smear positive pulmonary tuberculosis. As per the diagnostic algorithm being followed, TB symptomatic who turn out negative for TB on sputum smear, are prescribed 14 days of antibiotics following which they undergo Chest X-ray to rule out TB. Majority of TB symptomatic found smear negative do not return for chest X-ray after 14 days of antibiotics and are thus lost.

Intervention or response: Population Services International (PSI) actively followed up on smear negative TB symptomatic at intervention Designated microscopic center (DMC) in Barmer district of Rajasthan, India, and mobilized them for upfront chest X-ray instead of after 14 days of antibiotics. Trained community volunteers traced the smear negative TB symptomatic and ensured that they underwent Chest X-ray at the earliest. The Medical officers at DMCs verified the Chest X-ray reports of qualified radiologists.

Results and lessons learnt: We compared results of Quarter 4-2014 with Quarter 4 2015 from the PSI intervention DMCs in Barmer. In Quarter 4-2015 total 53 smear negative TB symptomatic underwent chest X-ray as against 13 smear negative TB symptomatic in the same quarter of 2014. In Quarter 4 2015, 21 (40% of those who underwent chest X-ray) smear negative TB symptomatic were diagnosed as having TB by chest X-ray as compared to 4 (31% of those who underwent chest x-ray) in Quarter 4 2014.

Conclusions and key recommendations: Active following-up of all smear negative TB symptomatic and subjecting them to Chest X-ray at the earliest, instead of waiting for completion of 14 days antibiotics, reduces loss to follow up and increases detection of TB among smear negative TB symptomatics.

PD-888-28 Strengthening patient-centered care by implementing a TB-HIV active surveillance system in Swaziland

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Background and Challenges to Implementation: Swaziland has a tuberculosis (TB) incidence of 733/100 000 with drug-resistant TB prevalence of 7.7% and 33.7% among new and previously treated patients, respectively. Compounding the challenge is an HIV prevalence of 26% and TB-HIV co-infection rate of 80%. The country's forceful response to the dual-burden resulted

in accelerated access to treatment necessitating the establishment of a robust pharmacovigilance (PV) system. The Ministry of Health (MOH) established an active surveillance system, in June 2013, focusing on patients initiating new TB regimen and antiretrovirals (ARVs.). Nonetheless, with staff rotation, attrition and fatigue, the quantity of patients enrolled on active surveillance and quality of adverse drug event (ADE) reports declined. There was also need to use the available information to improve patient-care.

Intervention: The MOH, with support from the USAID-funded Systems for Improved Access to Pharmaceuticals and Services program (SIAPS) formally established a National Pharmacovigilance Unit within the MOH, which: 1) Reviewed the PV system tools to make them more comprehensive. 2) Conducts re-sensitization trainings and monthly supportive supervision visits to implementing facilities. 3) Conducts quarterly data analysis, causality assessment and information dissemination. 4) Developed three job aids to improve reporting rates and standardize the identification and grading of ADEs. 5) Developed ADE management guidelines aligned to the Swaziland Essential Medicines List to improve ADE management and limit patient out-of-pocket medicines-expenditure.

Results: Comparing pre-implementation (August 2014-February 2015) and post-implementation findings (March 2015-September 2015), the patient enrolment rate onto the system increased by 58% and the ADE reporting rate increased by 83%. Causality assessment showed improved ADE reporting quality, with 95% of ADEs reported being probably/possibly caused by the medicines (an increase from 90% in February 2015).

Conclusion: Swaziland effectively established an integrated pharmacovigilance system to reduce risks associated with ADEs, improve ADE management and patient safety. Due to improved data accuracy, the data on ADEs for TB patients on second line treatment was used to quantify the number of patients who will require bedaquiline due to toxicities. The results are also being used to generate a risk profile to inform treatment guidelines for co-infected patients.

PD-889-28 Cost and operation management of a community outreach program improving access to TB care services in tribal populations in Central India

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Background: To improve access to tuberculosis (TB) care in the Saharia tribes of Madhya Pradesh province, India, project Asha Kalp (AK) implemented a community health workers (CHWs) based active case finding (ACF) and TB treatment delivery and monitoring (TDM) program since July 2014. Given its potential to

address TB care accessibility in similar rural areas, costs and impact on existing healthcare infrastructure must be evaluated for the programs sustainability and scalability.

Method: We evaluated incremental cost of implementing AP program using top-down macro-costing method. Complete operational expenditure of AK during 2015 calendar year was assessed and classified as direct and indirect costs. These were then allocated for each type of per services provided (ACF and TDM) based on total number of CHW visits needed per patient for each service. In order to quantify time require to complete each services provided by the CHWs, we conducted a time and motion (TAM) study, directly observing CHWs daily activities during the month of March 2016.

Results: Between January and December of 2015, 23 CHWs screened a total of 76 632 person, identifying 7216 persons suspected of TB infection. Of the 5652 persons providing sputum for diagnosis, 1662 new TB patients (829 smear positive and 830 smear negative patients) were identified and received DOTS from CHWs. Based on our pilot TAM study, CHWs covered an average of 95 km in distance (accounting for 56% of total work time), screened an average of 10 person, and administered DOTS to 6 patients per day. Based on our preliminary cost analysis, unit costs of screening, diagnostic visits, and delivering DOTS treatment were \$0.22, \$1.05, and \$51.05 per patient. Cost to identify one smear positive patient was \$8.26 and to identify and treat one TB patient was \$55.17 (drug and health services costs excluded).

Conclusions: Initial findings from our study suggests that the AP model has a potential to be highly cost-effective in addressing TB care problems in remote rural India. However, given considerable increase in sputum sample submitted and TB patients identified, AP's impact on existing public health system infrastructure must be assessed to better assess the program's sustainability.

PD-890-28 Improving case management with integration of TB patient management into hospital software in Viet Nam

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Background and challenges to implementation: Viet Nam is a high TB and MDR-TB burden country. All 63 provinces and 713 districts have health facilities with TB diagnostic and treatment capacity. All these facilities record TB and MDR-TB cases in National TB Program (NTP) paper logbooks. The paper based recording is time-consuming and difficult to track cases for early treatment initiation.

Intervention or response: Between April 2014 and December 2015, the USAID's TB CARE II Project, in collaboration with the NTP, implemented FAST - a new strategy to early detect, diagnose, and initiate effective treatment of infectious TB cases - at Nam Dinh Provincial Hospital of TB and Lung Diseases. The

hospital was supported to deploy the first hospital software which incorporated TB and MDR-TB patient management. The software facilitated quick detection of presumptive TB cases with TB suspecting X-ray and presumptive MDR-TB cases, which were prioritized for Xpert testing. Xpert testing had been available on site since January 2015. The software automatically generated NTP logbooks with higher accuracy and reduced recording time and logbooks for timely follow-up of lab results with bacteriological confirmation to early initiate regimens.

Results and lessons learnt: The number of MDR-TB cases increased from 22 to 29 in 2014 and 2015 respectively. The average number of days from patient visit to MDR-TB treatment initiation was reduced from 30.7 in 2014 to 12.2, 9.5, 8.6 and 6.3 in the quarters of 2015: January-March, April-June, July-September and October-December, respectively. The average number of days from receipt of specimens to MDR-TB treatment initiation was also reduced from 24.6 in 2014 to 4.2 in 2015. The number of bacteriologically confirmed pulmonary TB also rose from 303 in 2014 to 425 in 2015. The average number of days from patient visit to TB treatment initiation for 68 smear-negative pulmonary TB cases was 7.9, compared to 9.5 for 208 other smear-negative pulmonary TB cases. These time indicators automatically calculated on individual cases facilitated timely monitoring and performance improvement.

Conclusions and key recommendations: The first hospital software incorporating TB and MDR-TB patient management was successfully deployed to timely follow up cases for early treatment initiation at the selected setting.

PD-891-28 Out-patient treatment of TB patients in the Kyrgyz Republic

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Background and challenges to implementation: In 2011, a new technology in TB detection, Xpert MTB/RIF was launched in the Kyrgyz Republic. As the National Program Den Sooluk included implementation of full outpatient treatment of TB patients, the Ministry of Health initiated testing of a full ambulatory model in Issyk-Ata rayon with the total population 138 000 and high TB incidence, 136 cases per 100 000. The Xpert MTB/RIF was considered to be a strategic approach for the outpatient model for TB patients in the country.

Intervention or response: The diagnostic algorithm for the pilot rayon was created. It included sputum testing on Xpert MTB/RIF. Criteria for hospitalization based on modern WHO recommendations on TB were developed. All PHC medical staff was trained on selection of TB suspects, sputum collection, new diagnostic algorithm and ambulatory treatment of TB patients. All TB patients were tested on Xpert MTB/RIF. Based on the Xpert MTB/RIF results, rayon TB specialist make decision and

offer patients take TB treatment in PHC settings and patients with resistant form were sent to TB hospitals. All TB cases were registered in current TB registers. Also, data was put into the electronic data base on Excel program. The cohort consisted from 226 TB patients registered and treated in Issyk-Ata rayon. Two groups of patients were formed: 1) outpatient model ($n = 70$), 2) control group ($n = 156$), patients treated in hospital. TB patients of different categories in two groups were presented in relatively equal proportions.

Results and lessons learnt: Treatment success of smear-positive patients in two groups was 86% and 81% ($P < 0.001$). The overall treatment success rate of all patients in group 1 was significantly higher (96%) compared to group 2 (79%) ($P < 0.05$).

Conclusions and key recommendations: Xpert MTB/RIF may be successfully implemented at primary healthcare level and should be considered as a strategic component of integration of TB services at PHC level. Outpatient TB treatment model may be successful in the Kyrgyz Republic. Based on pilot results the Ministry of Health developed a National plan on the implementation of ambulatory model in the country.

PD-892-28 Medical college's contribution in ensuring universal access to TB care in India: a case study from an Indian state

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Background and challenges to implementation: Revised National Tuberculosis Program (RNTCP) in India in 1997 recognized the role of medical college in providing comprehensive TB care services and now is the largest national health program globally to have documented contribution of medical colleges in program implementation. Himachal Pradesh State (population 7 million) has two strategically located medical colleges (IGMC Shimla and RPGMC Tanda). During initial years of RNTCP launch in Himachal, the program faced several challenges in service delivery, capacity building, infrastructure and skilled human resource. Medical college's involvement provided solutions to many of the problems; as a result, program has been achieving its objective of case detection and cure rate for last several years. This study documents the functioning of medical colleges for implementing RNTCP and their contributions.

Intervention or response: A State Task Force (STF) at state level and core committees in both medical colleges were formed to implement and review the program. DMC cum DOTS centres were opened in both colleges with an objective to provide the quality assured diagnosis and standard treatment. Series of trainings conducted both at national and state level. Diagnostic and treatment services for MDR-TB cases established both medical colleges.

Results and lesson learnt: Medical colleges in Himachal Pradesh contributed in a major way in finding more TB

cases. Between 2012-2015, both medical colleges contributed near 15 % of total case finding, 10% of smear negative and 40% of extra-pulmonary TB cases in the state. Medical college faculties are earnestly following RNTCP guidelines. State Task Force in last 4 years supported 09 PG dissertations on RNTCP. Besides this, 13 major operational research projects and 11 small term operational research projects were conducted by the undergraduates with support from STF.

Conclusions and key recommendations: There is a systematic involvement of medical colleges in RNTCP implementation in Himachal Pradesh. However, in view of providing Universal access to quality TB care and meeting new targets under National Strategic plan 2012-2017, medical colleges has to play bigger role in capacity building, service delivery by improving coordination and operational research.

29. Community-based, decentralised MDR care

PD-893-28 Addressing the challenges of drug-resistant tuberculosis and other TB treatment outcomes in selected local government areas in Nigeria

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Background: Poor TB treatment-outcomes including multi-drug resistant-TB (MDR-TB) are emerging Public Health threats in Nigeria. In order to identify effective strategies to improve TB treatment-outcomes, we analyzed the role of selected Treatment Supporters (TS) in our Government-led Community-TB Care (CTBC) program.

Methods: With funding from PEPFAR, through USAID, FHI360 in collaboration with NTBLCP Nigeria actively introduced community-based treatment-support services by Community Volunteers (CV) through its CTBC program in 34 high burden TB-HIV LGAs in Nigeria in October, 2013. Selected CV including family-members of TB-patients were trained using an integrated-TB training curriculum, and subsequently engaged as TS to provide services including home-visits, health-education, daily DOTS, Infection-Control measures, psychosocial and nutritional interventions to beneficiaries on TB-treatment in the community. Government Health-Care Workers were also trained on effective TB-management. Records of TB patients on treatment 24-months before introduction of treatment-support services (pre-intervention) and 24-months after, (Intervention) were retrospectively analyzed and compared for treatment-outcomes. Based on WHO definition, treatment-outcomes were interpreted as successful if patients completed the 6

months TB-treatment regimen and achieved a cure, while treatment-failure, default, death, and MDR-TB diagnosed by GeneXpert and Sputum Culture were unsuccessful outcomes. Data analysis was done using SPSS version 16.

Results: Of the total 1946 TB cases (1128 Males, 818 Females) in the pre-intervention group, 1615 (83%) achieved a cure, 174 (8.94%) died, 38 (1.95%) defaulted and 119 (6.12%) were diagnosed to have MDR-TB. Seventy nine (4%) of these total were co-infected with HIV. Out of the total 3663 (2271 Males, 1392 females) in the intervention group, 3350 (91%) achieved a cure, 154 (4.20%) died, 137 (3.74%) defaulted and 22 (1.41%) had MDR-TB. Five per cent (183 cases) of these total were TB-HIV co-infected. This shows an 8% increase in cure rate ($P=0.000$), 4.74% decrease in death rate, ($P=0.393$), and 4.71% decrease in the rates of patients diagnosed with MDR-TB ($P=0.000$) with treatment-support services than without.

Conclusions: Targeted community-based treatment-support services are effective and low-cost strategies for improving TB treatment-outcomes in countries with high TB-HIV and MDR-TB burden. However, in-depth studies in similar resource-limited populations, to identify predictors of unsuccessful TB treatment-outcomes are recommended.

PD-894-28 Unraveling on-treatment mortality at a decentralized DR-TB hospital in KwaZulu-Natal, South Africa

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Background: KwaZulu-Natal suffers the highest burden of TB and HIV in South Africa. Despite decentralized MDR-TB care since 2008 and Xpert MTB/RIF implementation in 2013, on-treatment MDR-TB mortality is rising. We sought to characterize on-treatment mortality in a rural decentralized MDR-TB treatment facility.

Methods: We reviewed charts of laboratory confirmed MDR-TB patients who initiated treatment in 2015 and subsequently died. Additionally, using clinic registers, we compared non-survivors and survivors with respect to gender, prior TB, HIV status, and antiretroviral therapy (ART) status.

Results: Among 138 MDR-TB treatment initiators in 2015, 29 (21.0%) had died when data were censored (censoring at mean 232 days from initiation). Those who died had median age 36 (IQR 29-49) and included 13 (45%) men. Nine (31%) had received prior TB treatment. Fourteen (48%) had smear-positive TB. All patients who died were diagnosed with Xpert and

treatment was initiated a median of 8 days after diagnosis. Twenty-six (90%) were HIV-positive with median CD4 count of 31 cells (IQR 18-96); most had oral thrush ($n=17$; 59%) or chronic diarrhea ($n=8$; 28%). Twelve (41%) were previously on ART (median time of 9.3 months, IQR 2.5-45.1) and an additional 7 (24%) started ART during MDR-TB treatment.

Patients who died had low median hemoglobin [9.7 g/dL (IQR 6.6-11.6)], albumin [24 mmol/L (IQR 19-26)], and BMI [19.7 (IQR 17.0-22.7)] on admission. Seven (24%) had elevated creatinine at baseline, and 15 (52%) had at least one elevated creatinine prior to death. Median time on treatment before death was 50 days (IQR 15-87). In a preliminary analysis, compared to survivors, gender ($P=0.28$), prior TB ($P=0.57$), and HIV status ($P=0.55$) were not significant, but lack of ART prior to MDR-TB diagnosis was significantly associated with mortality ($P=0.05$).

Conclusions: Despite efficient linkage following Xpert, patients who died presented with a clinical phenotype of advanced HIV, anemia, hypoalbuminemia and renal failure, suggesting late presentation to care. To reduce unacceptably high mortality, in addition to early MDR-TB case detection and ART, critical care should not be neglected. Further investigation and investment are needed to strengthen our capacity to care for severely ill patients embarking on MDR-TB treatment.

PD-895-28 Decentralization of MDR-TB cohort reviews to regional level improves participation of key stakeholders: lessons from enhanced regional cohort reviews in Uganda

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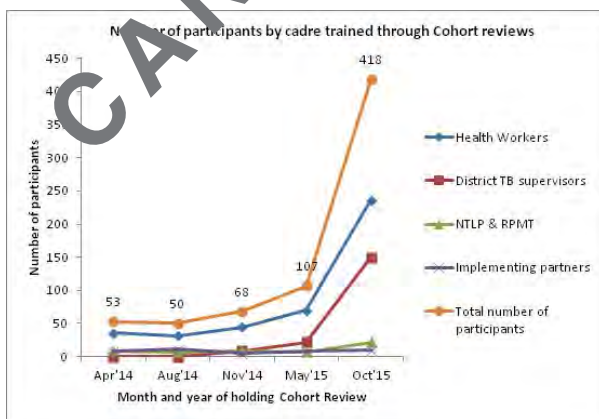
Background: Uganda's new and retreatment TB patients are estimated to have 1.4% and 12.1% MDR-TB. About 250 MDR-TB cases initiated on treatment prior to 2014 had not been evaluated mainly due to lack of trained health workers and logistical funding. National TB and Leprosy Program (NTLP) decentralized their treatment evaluation amidst challenges including low awareness of MDR-TB management. We explored the benefits of decentralizing cohort reviews (CR) to the regional level in order to increase participation and skills of stakeholders.

Intervention: USAID funded TRACK TB project and NTLP organized 2 CR in April and August 2014 to systematically evaluate MDR-TB patients outcomes and document good practices. Demographics, clinical status, drug adherence, side effects, social challenges. Although capacity of participants to give care to patients was built, few could attend due to limited resources. Lessons on how to improve participation of multi-disciplinary care teams and skills transfer were learnt, Regional Performance Monitoring Teams (RPMT) underwent CR training and simulation exercises before next 3 CR meetings were held at regional level.

Lessons learnt: The following were achieved on MDR-TB between April 2014 and October 2015: 1) Capacity to organize and manage CR was improved in the country from 5 to 22 officials; 2) Multi-disciplinary care teams accountable and motivated to give care improved from 32 to 236; 3) Implementing partners involved in creating awareness at a regional level increased from 2 to 29 leading to improved patient management and identification of contacts; 4) Proportion of patients getting lost to follow up reduced from 17% to 7% due to better community awareness and case management by health workers; 5) District Local government involved in MDT-TB activities increased from 0 to >50.

Conclusion: Results highlight the critical role of regionalizing CR to improving participation and awareness among key stakeholders.

Figure Participants trained



PD-896-28 Interim treatment outcome among patients managed for drug-resistant TB in three treatment centres in Nigeria

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Background and challenges to implementation: Drug resistant TB (DR-TB) is becoming a big public health problem in Nigeria with a DR-TB prevalence of 2.9% among new cases and 14.3% among retreatment cases in the DRS of 2012. Treatment outcome studies in managing the disease in Nigeria is scarce. Sputum culture-conversion, deaths, defaults to treatment are possible outcomes following intensive phase of DR-TB treatment. FHI 360 was supported by PEPFAR through USAID under the terms of Strengthening Integrated Delivery of HIV/AIDS (SIDHAS) to support management of DR-TB in 3 states of Nigeria. We describe the interim treatment outcome among patients managed for intensive phase in 3 large DR TB treatment centers in Nigeria supported by FHI360.

Intervention or response: Routine clinical and lab records of DR-TB patients on intensive phase of treatment in Lagos, Kano and Cross River states of Nigeria, between April 2011 and June 2015, were retrospectively analyzed. Data on patient demographics, weight, HIV status, Xpert MTB/RIF, baseline sputum culture and follow up results were entered into CS Pro.

Results and lessons learnt: A total of 267 patients met the inclusion criteria (56 were negative from baseline, hence, removed from further analysis). Of these, 69% (183) were males and 62% (166) were between 25-44 years, the median age of study participants was 34 years (IQR 28-44). Median weight at baseline was 51 kg (45-57), 70% (98) weighed 41-60kg. Majority (63%) of the patients were category II failure patients, 11% were HIV-infected. GeneXpert and culture results at baseline were positive in 99% (263) and 96% (255) respectively. Variations in GeneXpert and culture results at baseline occurred in only 1 patient (0.4%). Majority of the samples sputum converted (92%), 6% died, 1% defaulted and 1% did not sputum convert. The median time to culture conversion was 2months (IQR 1-4). Time to culture conversion was 3 months or less for 134 (57%) patients.

Conclusions and key recommendations: This study demonstrates a successful interim treatment outcome among a cohort of DR-TB patients being managed in Nigeria. There was no significant difference in culture conversion on the basis of HIV status.

PD-897-28 Follow-up of multidrug-resistant tuberculosis patients enrolled in the home care project of a community health department in a tertiary care hospital in Delhi

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Background and challenges to implementation: The World Health Organization/International Union Against Tuberculosis and Lung Disease's global survey in 1998 had revealed that multidrug-resistant tuberculosis (MDR-TB) is already a global pandemic, with local hot zones of increased transmission in several countries. To realize the vision of a world free of TB it becomes mandatory to disallow treated TB and MDR-TB patients to have relapse or become XDR cases. There is no policy under RNTCP for Long term follow-up. Long term follow-up of treated cases who also received home care and counseling hasn't been done thus far in India. Our hypothesis is that treated cases of MDR-TB in Delhi who received home based support with counseling are physically and mentally healthy after five years of registration under DOTs Plus.

Intervention or response: This retrospective study was carried out at Community Health Department of a tertiary care hospital of Delhi. It followed a project entitled Home care for MDR-TB patients. The study involved 109 ex-MDR-TB patients. These patients had

received treatment from their respective DOTS providers and home care and counseling support from CHD, starting from August 2009 till August 2010. They completed MDR treatment by August 2011 to 12. The study period is from August 2009 to August 2015.

Results and lessons learnt: One hundred and nine MDR-TB patients treated in Delhi, India under the project on Home care were followed-up for a median of 71 months. Out of 109 patients in 2009 to 2015, 66.9% were healthy, 23.9% dead, 3.7% defaulters, 3.7% failure cases whereas 1.83% had relapsed after long follow-up. The mental status and nutritional status also improved significantly immediately post treatment completion and five years after the treatment ($P < 0.001$).

Conclusions and key recommendations: Our study concludes that treated cases of MDR-TB who received home based support with counseling are physically and mentally healthy after five years of registration under DOTS Plus. At present, there is no mechanism under RNTCP to follow up treated cases of MDR-TB. We recommend that RNTCP comes up with such a mechanism. Continued contact of ex-MDR-TB patients will further reduce Loss-To-Follow-Up thereby reducing the spread of MDR-TB.

PD-898-28 Survival and predictors of mortality among multidrug-resistant tuberculosis patients on treatment in two regions of Ethiopia

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Background: It has been about four years since Ethiopia started to treat multi-drug resistant TB (MDR-TB) patients using second line drug (SLD) treatment by ambulatory model of care. We present the survival analysis for the initial one year cohort of MDR-TB patients on follow up in eight health facilities.

Methods: A retrospective cohort study was conducted among cohorts of MDR-TB patients who initiated SLD treatment during April-September 2012. Time to death during TB treatment was the measure of MDR-TB treatment outcome. We used Kaplan Meier method to estimate and graph survival probabilities as a function of time, and Cox regression analysis to determine hazard ratios (HR) with 95% confidence intervals (95%CI).

Results: Data was analyzed for a total of 90 MDR-TB patients followed for 30 527 person-days. Median follow up time was 608 person-days. There were 32 death followed for 614 person-days. The respective survival rates at 1, 3, and 6 months was 90%, 76.4% and 68%. Survival rates at the end of intensive phase for the age groups of < 25 years, 25-40 years and ≥ 40 years were 80%, 65% and 44%, respectively ($\chi^2 = 4.5$; $P = 0.03$) (Figure). There was a 3% increase in the rate of death for every one year increase in the age of MDR-TB patients (Table).

Conclusion: Mortality rate of MDR-TB patients in this study is lower than most studies in Ethiopia. However, close clinical monitoring is essential during the intensive phase of MDR-TB treatment that might target older ages.

Table Cox proportional hazard model

Patient attributes	Unadjusted HR (95% CI)	P value	Adjusted HR (95% CI)	P value
Sex (female/male)	0.84 (0.42-1.70)	0.63	0.87 (0.43-1.78)	0.71
Age, years	1.03 (1.003-1.06)	0.03	1.03 (1.003-1.057)	0.03
BMI, kg/m ²	0.98 (0.89-1.07)	0.65	0.97 (0.87-1.07)	0.50
HIV status (HIV+ve/HIV-ve)	1.71 (0.82-3.55)	0.15	1.58 (0.74-3.35)	0.24

PD-899-28 High retention in a community-based MDR-TB program in Haiti

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Background: Rising rates of multidrug-resistant tuberculosis (MDR-TB) threaten global tuberculosis (TB) control. Few patients receive effective therapy and cure rates are low due to high rates of attrition and mortality. For patients treated in inpatient settings, hospitalization consumes a large portion of the budget with unclear clinical benefit. We evaluated treatment outcomes before and after switching to shorter hospitalization times for patients with MDR-TB in Haiti.

Intervention: From 2008 to 2012, patients were hospitalized at the Haitian Study Group for Kaposi's Sarcoma and Opportunistic Infections (GHESKIO) for MDR-TB treatment for approximately 10 months until achieving 6 consecutive negative cultures followed by outpatient therapy to total 24 months. In 2013, the protocol changed with patients hospitalized until achieving 2 consecutive negative cultures (4 months). Outpatient treatment includes supervision by a family member and twice-daily directly observed therapy (DOT) by clinic staff, with global positioning systems (GPS) and camera-equipped smartphones to document adherence. Patients are provided with transportation fees and phone cards to facilitate communication with clinic staff. There are monthly support meetings with patients and families. Patients receive a monetary reward of \$US 200 upon completion of therapy.

Results: From 2008 to 2012, 108 patients received MDR-TB treatment at GHESKIO with hospitalization for 10 months. From 2013 to 2015, 150 MDR-TB patients were hospitalized for 4 months. Of those hospitalized for 10 months, 25 (23%) were HIV co-infected; of those hospitalized for 4 months, 30 (20%) were HIV co-infected. Among patients hospitalized for 10 months, 82 (76%) completed treatment/cure, 18

(17%) died, and 8 (7%) were lost to follow-up (LTFU). Among patients hospitalized for 4 months, 42 (28%) completed treatment/cure, 87 (58%) are still on treatment, 15 (10%) died, and 6 (4%) were LTFU. Rates of death and LTFU were lower among patients hospitalized for the shorter period ($P = 0.039$).

Conclusions: Initial hospitalization time for MDR-TB patients can be shortened without worsening clinical outcomes. We attribute the high rate of retention in MDR-TB treatment to social support, twice daily DOT, and financial incentive to complete treatment. Steady improvement in clinical success has been achieved despite the devastating earthquake of 2010.

PD-900-28 A new child on board: nurse-initiated MDR-TB treatment

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Background: Not only does South Africa have the largest number of people living with HIV, but also has the third most people with multidrug-resistant tuberculosis (MDR-TB) infection. Before 2011, National Guidelines mandated that patients with drug resistant TB be hospitalized and started on treatment. With only a handful of specialized TB hospitals at the time, new cases quickly outstripped bed capacity. This was compounded by a shortage of doctors, and the country implemented a decentralized approach to manage MDR TB patients. Subsequently, South Africa became the first country to implement nurse-initiated management of MDR TB. Targeted outcomes of this approach was evaluated.

Methods: A retrospective cross-sectional descriptive record review was conducted among 7 decentralized MDR-TB units to compare doctor and nurse MDR-TB management and looking at key early outcome indicators over a 15 month period. Data of 5081 MDR-TB patients started on treatment were analysed.

Results: In total, 5081 MDR-TB patients were included for analysis. Of these 599 (11.8%) were managed by nurses, and 4482 (88.2%) managed by doctors. The mean age of 36.87 years for patients managed by nurses was slightly higher than those managed by doctors (35.05). 2642 (52.04%) in the cohort were males and 2437 (47.96%) females. 4606 (90%) of patients knew their HIV status, of which 576/599 (96.1%) and 4030/4482 (89.9%) were nurse- and doctor-managed, respectively. Known sputum results did not show a significant difference when comparing conversion rates among nurses initiated, 224/559 (37.40%) and doctor initiated, 1728/4482 (38.55%) patients. Further, of the mere 29% of legible patients started on Cotrimoxazole Preventative Therapy (CPT), 256/470 (54.47%) were nurse-managed and 1476/3071 (39.73%) doctor-managed ($P < 0.01$). The proportion of patients started on Antiretroviral Therapy (ART) were (2821/3071) 91.57% among

patients managed by doctors, and (363/470) 77.2% among those managed by nurses ($P < 0.01$).

Conclusions: Known sputum results did not show a significant difference in outcomes between doctor and nurse managed patients. CPT uptake remained poor, though nurses tended to start more patients on CPT, while more patients were initiated on ART's when managed by doctors, when compared to those managed by nurses. Further research is required.

PD-901-28 Interim treatment outcomes of clinic-based ambulatory care of MDR-TB patients initiating treatment at the Mulago Hospital MDR-TB Clinic, Kampala, Uganda

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Background: Uganda is faced with a high burden of Human Immunodeficiency Virus (HIV) infection and multidrug-resistant tuberculosis (MDR-TB). To address the issue of costs of hospitalization and limited space due to the growing numbers of MDR-TB patients that seek treatment from Mulago Hospital MDR-TB clinic, clinic-based ambulatory care has been adopted. The World Health Organization (WHO) recommends ambulatory treatment for MDR-TB and most national TB programmes have adopted an ambulatory strategy. In this study, we report the interim treatment outcomes of clinic-based ambulatory care of MDR-TB patients initiated from Mulago Hospital MDR-TB clinic Kampala.

Methods: In this retrospective cohort study, we reviewed the patient records of all MDR-TB patients initiated on treatment between 1 January 2013 and 31 May 2015. We determined the proportions of MDR-TB patients who had culture conversion (main outcome), those who died and those who were lost to follow-up by the end of the first 6 months on treatment. The χ^2 test was used at bivariate to appropriately determine factors associated with culture conversion by the end of the first 6 months on treatment. At bivariate analysis, variables that were significant at $P < 0.2$ were selected for multivariable analysis. At multivariable analysis, variables that had $P < 0.05$ were considered significantly associated with culture conversion.

Results: Of 246 patients, 155 (63%) were male, median age was 32 years and 116 (47%) were HIV-infected; all 116 HIV positive patients are on CPT and ART.

Generally, 197 (80%) were alive and culture negative at the end of the first 6 months on treatment, 42 (17%) died and 7(3%) were lost to follow-up. 39/42 (92%) cases who died were MDR-TB-HIV co-infected. Infection with HIV ($P = 0.01$) and prior history of anti-tuberculosis drug use ($P = 0.02$) were significantly associated with culture conversion.

Conclusions: Outcomes of clinic-based ambulatory care were similar compared with previously published data from international cohorts, thus confirming the effectiveness of this approach. However, majority of those who died were MDR-TB-HIV co-infected, so much

attention should be dedicated to those co-infected. We recommend that MDR-TB-HIV co-infected patients should be hospitalized for a specific period of time so as they are closely monitored before adopting ambulatory model of care.

PD-902-28 Low pre-diagnosis and pre-treatment attrition among adults with presumptive MDR-TB in Chennai, India: an operational research

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Background: The increase in multidrug-resistant tuberculosis (MDR-TB) poses a major threat to the control of TB. Worldwide studies have raised concern over high pre-diagnosis and pre-treatment attrition or delay in MDR-TB diagnosis and treatment pathway (DTP). Considering this, the International Union Against Tuberculosis and Lung Disease conducted an operational research across multiple districts in India. Here we report the findings of the study done in Chennai district. The specific objectives were to determine 1) among presumptive MDR-TB patients, the pre-diagnosis attrition and turn-around time (TAT) to get drug susceptibility testing (DST); 2) among confirmed MDR-TB patients, the pre-treatment attrition and TAT to start treatment; and 3) the factors associated with pre-diagnosis attrition.

Methods: The study was conducted in the Revised National Tuberculosis Control Programme setting. It was a retrospective cohort study involving record review of all eligible presumptive MDR-TB in 2014. Frequencies and proportions were used to summarize presumptive MDR-TB patients at each step of DTP. Median and interquartile range was used for TAT for each step. Relative risks (RR) and 95% confidence intervals were used to summarize and infer the factors associated with not getting the DST done.

Results: Of 605 presumptive MDR-TB patients, 534 underwent DST and 29 patients were diagnosed as having MDR-TB. Pre-diagnosis attrition and pre-treatment attrition was 12% (71/605) and 21% (6/29) respectively. Among those with pre-diagnosis attrition, 66% (47/71) were not identified by the programme. TAT [median (IQR)] to get DST and initiate DR-TB treatment after date of eligibility were 14 (8–25) and 36 (28–71) days respectively. Presumptive MDR-TB patients with extra-pulmonary TB [RR = 2.4 (1.2–4.5)] and those registered in the first quarter of 2014 [RR = 2.5 (1.3–4.5)] were less likely to undergo DST.

Conclusions: The programme tested most of the patients eligible for DST; however, there was scope for improve-

ment in preventing pre-treatment attrition. The TAT was satisfactory. DST among patients with extra-pulmonary TB needs special attention.

PD-903-28 Impact of community-based DR-TB program in reducing time to treatment initiation and increasing the number of enrollments

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Background and challenges to implementation: Immediate initiate of treatment after diagnosis of MDR-TB patients and enrolment of all diagnosed MDR-TB cases are the big challenges for MDR-TB programs globally. From late 2007, when the PMDT program was started in Bangladesh, a certain number of MDR-TB were diagnosed, but there was a huge delay in initiation of treatment due to a lack of treatment initiation centres. Again, a large number of cases were lost due to this long waiting time and created a huge gap between diagnosis and enrollment.

Intervention or response: A community based management approach was introduced in 2012 in Bangladesh and scaled up nationally by 2014. Efficient management of treatment initiation and early release of patients to community based treatment has resulted in a significant reduction in treatment delay and obtained enough space for enrolment of more patients which reduces the gap between diagnosis and enrolment.

Results and lessons learnt: The mean time difference between diagnosis and treatment initiation of MDR-TB patients in Bangladesh was increasing day by day since the starting of PMDT program which was 69 days in 2011. On the other hand, all the diagnosed MDR-TB patients were not being able to enroll under treatment, only 64% of total diagnosed cases were put under treatment in 2011. After introduction and scale up of community based management approach, the median number of days between diagnosis and treatment initiation has come down from 69 days in 2011 to 5 days in 2015 and also percent of enrolment sharply raised from 64% in 2011 to 95% in 2015.

Conclusions and key recommendations: The introduction of community-based management of MDR-TB patients has made a significant impact in reducing delay in treatment initiation and reducing the gap between diagnosis and enrolment. The programmatic results discussed above justifies the community based management as a cost-effective approach to increasing access to and providing quality-assured MDR-TB treatment.

30. Tobacco control: policy legislation

PD-904-28 The role of civil society in policy advocacy for tobacco control in Africa

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Background and challenges to implementation: The entry into force of the WHO FCTC in 2005 led to its rapid ratification by most African countries. However, the development of FCTC-compliant policies by African governments was slow and necessitated strong advocacy to speed the process. The African Tobacco Control Alliance (ATCA), a Pan-African network of over 125 civil society organizations (CSOs), implemented, as from late 2010, a Gates-funded 5-year project in 10 African countries to support the adoption of tobacco control (TC) policies.

Intervention or response: ATCA conducted in-country and regional trainings to build the capacity of influential groups in areas like advocacy, tobacco taxation and tobacco industry (TI) monitoring. Policy dialogues were held to mobilize support among policy-makers and high-profile media campaigns carried out to garner public support. Technical assistance was provided to governments in drafting TC legislation. Multi-sectoral teams were set up to monitor the TI. In West African Economic and Monetary Union (WAEMU), ATCA supported the integration of tobacco control in non-communicable diseases. All activities were carried out in close collaboration with government agencies and other key sectors.

Results and lessons learnt: Sustained advocacy and sensitization led to increased support for TC among decision-makers and influencers. The discrediting campaigns reduced the credibility and influence of the TI. These factors, combined, paved the way for the adoption of FCTC-compliant legislations in three countries; three other countries reached an advanced stage in drafting their TC bills. Tobacco taxes were increased in seven countries. Seven of the eight WAEMU countries have strategic plans on NCDs which include tobacco control.

Conclusions and key recommendations: The project contributed in creating a favourable environment for FCTC implementation in the target countries which, in the long term, will help in reducing tobacco-related morbidity and mortality and improving the quality of life of populations. It demonstrates that civil society represents a powerful force for policy advocacy and change. However, it should not work in isolation but partner with other organizations to achieve results. The project also shows that the tobacco industry, if not monitored and discredited, could easily derail tobacco control and the policy change process.

PD-905-28 How cigarette affordability can affect smoking prevalence in Brazil

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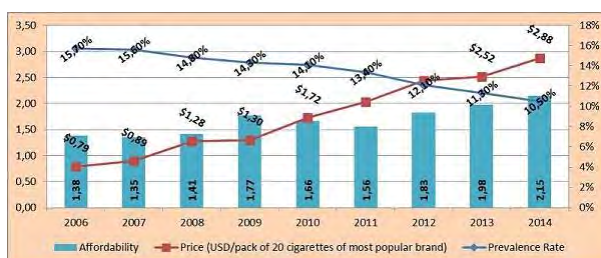
Background and challenges to implementation: Brazil has been implementing strong tobacco control measures since 1996 and reducing the cigarette consumption, but Brazilian cigarette has been considered one of the most affordable in the world and it could represent a threaten for national tobacco control policy.

Intervention or response: To implement the WHO Framework Convention on Tobacco Control Article 6 that provides measures relating to prices and taxes are effective and important means of reducing tobacco consumption by various segments of the population, the Brazilian government adopted in 2011 a measure that resulted in a 30% increase of the federal taxation on cigarettes and a policy of minimum prices for cigarettes. To evaluate the impact of this measure, we calculated the cigarette affordability rate in Brazil, considering that affordability refers to the price of the product in relation to income, as measured by the proportion of the annual per capita GDP required to purchase 100 packs of cigarettes of the most popular brand. The higher the index, the lower the economic access to cigarettes. We compared the evolution of affordability rate between 2006 and 2014 with the cigarette consumption based on the smoking prevalence data from the Risk and Protective Factors Surveillance for Chronic Diseases Telephone Survey (VIGITEL) in the same period.

Results and lessons learnt: This measure is the main responsible for raising the cigarette affordability by 37% between 2011 and 2014 and decreasing the smoking prevalence by 22 %, in the same period, according to data from VIGITEL. Tobacco is responsible for 36.9% of cancers deaths. Reducing the cigarette economic access can provide an important tool to avert the burden and the mortality of tobacco-related cancers in next decades.

Conclusions and key recommendations: Cigarette affordability level is more important than just the price and determines cigarette consumption. It has different levels comparing developing countries with developed ones where cigarettes are more expensive but the high levels of income make cigarettes more affordable. Strong and effective tobacco control policies, aligned with the affordability level leads to decrease cigarette consumption and guarantee the reduction of tobacco-related cancers and other diseases.

Figure Cigarette affordability and consumption



PD-906-28 The impact of the sin tax on health awareness programs

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Background and challenges to implementation: On December 2012, the Philippines enacted RA 10351 or the Sin Tax law, which was the result of 16 years of advocacy work to reform the tobacco excise tax system. The reasons for the reform are the following: 1) To help finance Universal Health Care program; 2) To simplify the current excise tax system on alcohol and tobacco products and fix long standing, structural weaknesses of the system; 3) To address the public health issues relating to alcohol and tobacco consumption. As a result, the budget for the Department of Health (DOH) increased tremendously starting in 2014. However, it was observed that among the identified Universal Health Care programs by the Law to benefit from the additional funds, health awareness remain severely under funded. The specific office/unit in charge was even downgraded resulting to a further fragmentation of health promotion efforts.

Intervention or response: The study made an analysis of the budget allocation and composition of the health awareness program and the other universal health care program items that benefit from the Sin Tax law.

Results and lessons learnt: The budget allocation for health awareness programs continue to decline despite the tremendous increase in the DOH budget. The paper found out that most of the sin tax funds were allocated to improve curative health services and provide more social health insurance. As a result, health promotion remain under appreciated as most of the funds were only spent to produce IEC or media materials.

Conclusions and key recommendations: In order to improve the utilization of the funds coming from sin tax, this paper recommends the following: 1) Review of the Medium-term Expenditure Framework (MTEF) of the DOH for UHC; 2) Reclassify the Health Promotion and Communication Service into a national bureau and increase the number of personnel; 3) Increase the budget for health promotion through the Sin Tax Fund.

PD-907-28 Impact of effective monitoring and regulatory mechanisms on vendors' compliance with ban on electronic nicotine delivery systems in Punjab, India

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Background and challenges: Electronic Nicotine Delivery Systems (ENDS or E-cigarettes) are growing in popularity as these are advertised as status symbols and unsubstantiated claims as cessation devices. In India, ENDS were declared unapproved drugs under Drugs and Cosmetics Act in year 2013. Under the Act, all the Drug Inspectors were instructed to initiate action in terms of filing court cases if any vendor is found selling ENDS/E-cigarettes. The objective of current study was to assess vendors' compliance to ban on ENDS/ E-cigarettes in a northern state of Punjab, India.

Intervention: Regular monthly monitoring of ban of ENDS/E-cigarettes at state level by Commissioner FDA and at District level by Deputy Commissioners is being done in Punjab. Strict implementation was done by seizing these products and launching court cases against seven violators of Drugs and Cosmetics Act immediately after the ban was imposed. Besides, health advisory was issued in the print media by Food and Drug Administration and e-commerce sites selling e-cigarettes were issued notices by State Tobacco Control Cell. A cross-sectional study was carried out in rural and urban areas of three selected districts of Punjab among the vendors who were selling tobacco products. A total of 300 tobacco vendors, equally distributed in three districts were interviewed. All establishments selling tobacco were assessed for compliance to ban on electronic nicotine delivery devices under Drugs and Cosmetics Act, based upon an observational checklist.

Results and lesson learnt: Only two of three hundred Points of Sale observed were selling ENDS/E-cigarettes, thereby violating the Drugs and Cosmetics Act. The vendors were of the view that tobacco users have not tried E-cigarettes as cessation devices.

Interpretation and conclusion: Strict monitoring and implementation of ban on E-Cigarettes by state and district level officials has resulted in an excellent compliance, which should be replicated in other states of India.

PD-908-28 Role of evaluation of internal tobacco industry documents in tobacco control: the case of Rwanda

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Background: Rwanda represents a good market opportunity for tobacco companies. Due to its geographical

location, it has been a base of tobacco industries rivalry and smuggling especially in the western part of the country. However, there are limited data about tobacco control in Rwanda and sub-Saharan Africa in general. This review of internal tobacco industry documents will potentially better inform tobacco control activists in Rwanda, other African and any countries that may have faced the same tobacco company promotion, marketing and illegal trade strategies.

Methods: A snowball literature search at legacy tobacco documents library was done, using different key words namely, Rwanda, tobacco market, tobacco brands, tobacco companies in Rwanda, smuggling. Documents were sorted by dates and only documents with the dates from 1986 were considered and finally seven documents were retained. Taking into consideration the realities on ground, two main themes emerged from the analysis of these documents.

Results: 1) Tobacco companies prospective about the Rwandan market: In their document entitled the East Africa Non Domestic Markets: Marketing Plans Secret, by the British American tobacco (BAT) company, an estimate of the size of the market was determined for nine countries: Sudan, Tanzania, Rwanda, Burundi, Somalia, Eritrea, Somaliland, Djibouti and Ethiopia. 2) Strategies of tobacco companies towards the Rwandan market: The competition in Rwanda has been high in the tobacco market since 1995, and tobacco companies have used local importers in order to secure their businesses. The government itself had shared 49% in the local manufacturer of tobacco and this was an opportunity for tobacco products to be promoted in the community. Further, tobacco industries were aware of the impact on sales of warning labels on tobacco products and had done research and none of these countries had apparent warning labels requirements.

Conclusions: Tobacco companies have invested a lot in market studies and have found ways of infiltrating governments using local operators and manufacturers. Such scenarios may have resulted in the BAT looking at ways of manipulating policy design and implantation that tobacco control activists are currently struggling with.

PD-909-28 Physicians' knowledge and practices regarding e-cigarettes in the USA: results from a national survey of primary care physicians

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Background: E-cigarette use is exponentially increasing in the USA. We attempted to assess the extent to which primary care physicians (PCPs) report recommending e-cigarettes and whether this is related to their knowledge.

Methods: We used a modified Dillman approach to administer a mailed survey to a national random sample ($n = 1430$) of office-based PCPs between February and

May, 2015. Survey content was informed by existing literature and qualitative research. The χ^2 tests were used for bivariate analysis to compare knowledge of PCPs who recommend and do not recommend e-cigarettes.

Results: 348 PCPs returned the survey for a 29% response rate. 57.8% ($n = 155$) reported previously recommending e-cigarettes to their patients who smoke. The majority reported recommending them for smoking cessation and harm reduction (71.6%, $n = 111$), 19.2% for smoking cessation only, and 9.6% for harm reduction only. Few PCPs (7.7%) answered all 5 knowledge questions correctly. Two-thirds (66.8% and 65.4%, respectively) of PCPs correctly knew that e-cigarettes were not currently regulated by FDA and that some e-cigarette brands can deliver more nicotine than traditional cigarettes, with the remainder choosing I don't know (26.6% and 28.2%, respectively). Almost half of the PCPs answered I don't know for the other knowledge questions: whether liquid in e-cigarettes can contain carcinogens, e-cigarettes could adversely affect lung function, and some e-cigarette brands do not deliver nicotine (44.1%, 52.7% and 46.7%, respectively), with only one third answering correctly (38.5%, 33.5% and 36.4%, respectively). PCPs were more likely to answer knowledge items correctly vs. otherwise if they had previously discussed e-cigarettes with their patients: 71.2% vs. 43.5% correct regarding FDA regulation ($P < 0.001$), 71.2% vs. 41.3% regarding delivering more nicotine ($P < 0.001$), 42.4% vs. 13.3% regarding e-liquid possibly containing carcinogens ($P < 0.001$), 42.4% vs. 13% regarding delivering no nicotine ($P = 0.001$). However, PCPs recommendation status did not vary by their knowledge.

Conclusions: The clear void in knowledge regarding the potential harms associated with e-cigarettes may be indicative of the influence that industry marketing may be having, as such marketing tends to focus solely on the potential benefits of e-cigarettes and is void of any risk communication or transparent product labeling.

PD-911-28 Misleading health claims of e-cigarette websites in Turkey

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Background: Turkish legislation bans internet sales of all types of tobacco products. Marketing, distribution, promotion and sales of electronic cigarettes are not legal. However, increasing number of electronic-cigarette websites have been recently reported. This study aims to investigate the content of electronic-cigarette websites in Turkish language.

Methods: This cross sectional observational study was carried out by google search for the key words of electronic cigarette or e-cigarette. Each detected website was analyzed with regard to the product ingredient information, health warnings, and smoking cessation

claims together with its reference institutions and literature.

Results: The google search revealed 96 electronic-cigarette websites in Turkish language marketing 53 various brands of e-cigarettes and 150 brands of e-liquid. Of those websites 56% did not disclose its trade identity. 41% did not provide any information about the amount of nicotine in the products sold or promoted. 88 % of the websites did not disclose the additives of the products. 62 % did not warn of the health hazards. 91% did not have any warnings for the use of minors. 51 % claimed their products to be safe. 56 % claimed that e-cigarettes helped to quit smoking. 26 % explicitly used the slogan 'makes you quit smoking'. Of all the websites, 20 % referred their health claims to recognized national and international institutions including, American Lung Association, National Cancer Institute, FDA, WHO and British Ministry of Health.

Conclusions and key recommendations: Electronic cigarettes which may be potentially hazardous to lung health, are marketed with misleading health claims. These websites must be screened and regulated. The international scientific institution whose reference are mentioned need to take action.

PD-912-28 E-cigarettes: prevalence of use and perceptions among adolescent college students in Mangalore city, India

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Background: Tobacco usage is the largest, preventable cause of premature mortality in the world. E-cigarettes are battery-powered devices that deliver vaporized nicotine without the tobacco combustion of regular cigarettes. Tobacco control advocates and researchers are concerned that e-cigarettes could act as 'gateway' devices, getting novice users, particularly the young people, addicted to nicotine and encouraging future tobacco use. The adolescent college students are a group, at risk for smoking initiation and may use e-cigarettes as an experimentation to start smoking. These products are gaining popularity in many countries but little is known about their use among students in India.

Methods: A descriptive cross sectional study was conducted on 1074 adolescent college going students of different pre-university colleges of Mangalore city using cluster sampling. Information was elicited on their socio-demographic characteristics, usage of e-cigarettes, perceptions and practices related to that. Statistical analysis was done using SPSS version 21.

Results: The mean age of study population was 16.4 years with 59% males. Around half of respondents (46.4%) had seen e-cigarettes advertised. A total of 16.1% reported trying an e-cigarette (5.1% nonsmokers, 18.4% former smokers, and 34.5% current smokers), and 5.9% reported use in the past 30 days. Compared to non-smokers, former smokers and current smokers were more likely to have tried e-cigarettes (OR 4.15 and OR

9.84, respectively), and current smokers were more likely to have tried e-cigarettes than former smokers (OR 2.37). Current smokers were also more likely to be current users of e-cigarettes than both former smokers (OR 15.24) and non-smokers (OR 4.83). Smokers were interested in trying e-cigarettes to help them quit smoking (80.4%), as a long-term replacement for cigarettes (74.8%), or to use in places where they cannot smoke (82.1%).

Conclusions: Most adolescent college students were aware of e-cigarettes, and a substantial minority reported trying them, with evidence of use among nonsmokers. Given that even experimentation with e-cigarettes could lead to nicotine dependence and subsequent tobacco usage, regulatory and behavioral interventions are needed to prevent 'gateway' use by adolescent college students. Education about e-cigarettes could help providers deliver comprehensive preventive services to adolescents at risk of tobacco use.

31. Tobacco epidemiology

PD-913-28 Comparison of direct and indirect estimates of current tobacco use status in 22 Global Adult Tobacco Surveys

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Background: In the recent past, credibility of Global Adult Tobacco Survey data (GATS) has been questioned. Current tobacco use information can be directly as well indirectly estimated in GATS, thus providing a wonderful opportunity to examine the validity to some extent. This study is focused on comparing the difference in current use estimation from different items of GATS.

Methods: The available GATS country data from CDC website were analyzed to assess the validity of respondent responses while revealing current tobacco use at different times of interview. Current smoking status can be directly estimated from item B01 and current smokeless tobacco use status can be directly estimated from item C01 of GATS tool. These estimates were compared with indirect estimates of current smoking status from item B01 and current smokeless tobacco use status from item C06.

Results: Difference in average daily smoking prevalence from direct and indirect estimates was in the range of 0.1–0.6% in 12 sets of country data. Similar difference (range 0.1–0.6%) existed in less than daily smoking prevalence in 19 data sets involving 17 countries when direct and indirect estimates were compared. The difference in daily smokeless tobacco use prevalence between direct and indirect estimations was 0.1% in Mexico and Philippines, 0.2% in Bangladesh and 0.8% in India. Similarly, out of 12 sets of data, in 5 sets of data from 5 countries had no difference for less than daily smokeless tobacco use estimates. In other sets of data, difference was ranged from 0.1% to 0.9%. Though the difference between estimates was <1%, in terms of

absolute numbers it can be a high for countries with larger population.

Conclusions: There is difference is direct and indirect estimates of current tobacco use in GATS. The full potential of using hand-held device for data collection in GATS needs to be explored as use of appropriate checks to validate the responses instantly by cross tallying the previous responses or with indicating input error in the handheld devices can improve credibility of data.

PD-914-28 A case control study of the prevalence of Green Tobacco sickness in two villages of rural Mizoram, India

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Background: Mizoram is a mountainous state of India, where agriculture remains the main occupation. Mizoram unfortunately boasts of having the highest tobacco use prevalence at 67.2%, with very high societal acceptance amongst both men and women of both smoke and smokeless tobacco. Tobacco cultivation is rampant in certain areas of the state, with a large percentage of people still dependent on tobacco cultivation as their sole livelihood. In this study two villages have been selected from Champhai district, one where tobacco cultivation is the norm (Buang) and the second village where tobacco is not cultivated (Hruaikawn). A survey was conducted among 100 adults in each village to find out if they suffered from complaints that could be attributed to Green Tobacco sickness (GTS).

Methods: A survey was conducted in the two villages using a questionnaire to evaluate whether respondents had complaints attributable to GTS as a result of being involved in tobacco cultivation and processing. In Buang where 90% of all households are involved in tobacco cultivation, respondents were divided equally so that 50% were directly involved in tobacco cultivation and 50% were not. In Hruaikawn village respondents were selected randomly from all households.

Results: The survey reports that various symptoms, which can be attributed to GTS as a result of handling tobacco leaves and processing it, are significantly higher in tobacco cultivators. As high as 70% of the tobacco cultivators suffered from at least 8 out of the 12 symptoms of GTS as compared to 41% of the control group in Buang and 30% in Hruaikawn. Reports were also received from some of the residents of Buang that they had changed their crop because they concluded that their health condition was compromised because of tobacco cultivation.

Conclusions: The study established strong correlation between tobacco cultivation and occurrence of symptoms suggestive of GTS. This is highly suggestive that occupation involving tobacco cultivation compromises

their health resulting in numerous complaints. It is arguable that symptoms of GTS are not very specific and cannot be attributed solely to tobacco cultivation, however the evidences strongly implicates tobacco cultivation and handling with reduced health status.

PD-915-28 A snapshot of tobacco use among adult populations in Punjab, India, using GATS protocol

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Background: Over one-third (35%) of adults consume tobacco products in different forms in India, the most common being smokeless tobacco (21%). Global Adult Tobacco Survey (GATS) 2009-2010 reports that current tobacco use in Punjab, India, is 11.7% (21.6% of males and 0.5% of females). After introduction of national legislation, namely the Cigarettes and Other Tobacco Products Act (COTPA), the Government of Punjab took various measures for its effective implementation in past five years, some of which included ban on e-cigarettes, chewable tobacco products, hookah bars and loose cigarettes. The present study was conducted with an objective to assess the tobacco use burden in the state of Punjab and determine the factors affecting tobacco use.

Methods: This cross-sectional study conducted in the period between December 2015 and March 2016 utilized a three stage sampling for collecting data from three randomly selected districts (administrative divisions) representing 3 major regions of Punjab, India. A sample size of 510 individuals was divided equally into urban and rural area with proportionate sampling on basis of subsets of age groups and gender. The questions based on Tobacco Questions for Survey (TQS), a subset of key question from GATS were used during interview with respondents. Ethical consent from Institution Ethics Committee was duly obtained prior to data collection.

Results: The overall tobacco use was 11.5%, with 23.1% among males (15.2% smoked and 7.8% smokeless) and none among the female population. The hand rolled cigarettes (bidis) constitute 64.1% of smoked tobacco. Tobacco use was high in urban areas (15.3%) as compared to rural areas (10%). Almost one third (33.3%) of the male population smoked 10-14 cigarettes on an average per day. High tobacco use was associated with higher age group (≥ 45 years), urban locality and person with low education background.

Conclusions: Prevalence of tobacco consumption is almost stagnant in the state of Punjab since last round of GATS in 2009-2010 which is an encouraging sign considering there is no further addition to existing cohort of tobacco users. Further strict implementation of COTPA and related legislation along with cessation efforts are needed to decrease the burden of tobacco use.

PD-916-28 An analysis of the opportunity cost of household expenditure on tobacco in Uganda's two lowest income groups

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Introduction: Tobacco control in Uganda is largely framed as a public health issue which limits its multi-sectoral and development policy imperative. We sought to re-frame tobacco control as a poverty reduction issue to enhance its policy agenda appeal. The objectives of the study were 1) To measure household expenditure on Tobacco by Uganda's two lowest income groups, 2) To compute the opportunity cost of household expenditure on tobacco with respect to potential purchases of selected food items.

Methods: Data were drawn from the most recent nationally representative Uganda National Household Surveys. Secondary data analyses of two combined Uganda household expenditure datasets of 2009/2010 and 2010/2011 were done. Potential purchases of selected alternative items with regard to selected food items were computed based on The Uganda Consumer Price Index of June 2010 after adjusting for inflation.

Results: Average monthly household expenditure on tobacco by Uganda's two lowest income groups was calculated at Uganda shillings 6364 (\$3.1). The overall average monthly expenditure on tobacco was higher in urban areas (7772 Shs/\$3.8) compared to rural areas (6160 Shs/\$3.0). Within the lowest two income groups, average monthly expenditure on tobacco decreased with increase in income. Tobacco-spending households spent less on eggs and consumed less litres of milk than the average household. The monthly household expenditure on tobacco would have potentially bought 8 litres of fresh milk or two loaves of bread and the equivalent of 3 and a half kilograms of maize flour—a staple food in Uganda.

Conclusion: Household expenditure on tobacco among the lowest two income groups in Uganda exacerbates poverty as it constitutes a significant sum that could potentially raise the nutritional status those households. We recommend that the rural-urban dichotomy in household tobacco expenditure be factored in tobacco control policy measures in Uganda. The study results offer the opportunity of an alternative advocacy dimension for tobacco control in low-income countries using local data from Uganda.

PD-917-28 Economic burden of tobacco-attributable diseases in India

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Background: Approximately 35% of adults in India uses tobacco in some form and it is responsible for nearly one

million deaths annually in India. Yet, there are not a single comprehensive study that estimate the economic burden from tobacco use in India. This paper estimates the economic burden of smoked and smokeless tobacco in India at the national and state levels.

Methods: The prevalence-based attributable-risk approach was used to estimate the direct medical costs, indirect morbidity costs and indirect mortality costs of smoked and smokeless tobacco using nationally representative household sample survey data from India. Costs due to all-cause mortality and four major tobacco-related disease—tuberculosis, respiratory diseases, cardiovascular diseases and cancers—were estimated at national level as well as for thirteen major states for males and females.

Results: Total direct and indirect costs of diseases attributable to tobacco use was INR 1045 billion (USD 22.4 billion) in 2011. Direct costs constituted 16% of these while costs from smoked tobacco contributed 78%. Female share in the costs attributable to smokeless tobacco was several times more than their share in the costs of smoked tobacco. Attributable costs from cardiovascular diseases comprised 37% of the costs from the four diseases combined. Among the 13 major states studied, 50% of the costs were shared by Uttar Pradesh, West Bengal and Andhra Pradesh.

Conclusions: The estimated economic burden was 1.16% of India's GDP and 12% more than the combined state and union health expenditure during 2011-2012. The direct medical costs alone came to 4.77% of total health expenditure and 18% of the total government health expenditures in India. Total excise revenue from tobacco in 2011 amounted to only 17% of the economic burden. Substantial variation in costs across states warrants targeted public health policy on tobacco in India.

PD-918-28 What GATS, India, has to say on female tobacco use initiation. What insights can we draw to halt this trend?

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Background: Tobacco use is rising in epidemic proportions worldwide. WHO estimates 80 000-100 000 people initiating tobacco on a daily basis, and significant among them are females. In India, an increasing trend of tobacco use among females is seen. At early ages, addiction is stronger, making them life-long users. Thus preventing experiments, initiating and regular use among females is a vital strategy of tobacco control efforts. A secondary analysis of the disaggregated publically accessible data (the Global Adult Tobacco Survey-GATS, India 2009-2010) was done for the adult population age ≥ 15 years. Only valid responses were considered. GATS reported initiation of tobacco use among males and females at age of 12 years. More females (5%) started smoking at age 12 than men (3%) at the same age. 12% of females started using smokeless tobacco products at age of 12 years as opposed to 4% of males. Also data

show that 44% females started dual tobacco use at same age compared to 32% of males.

Policy Intervention: While implementing the 85% graphic warnings (PHW) we can increase the efficacy among users to increase knowledge and their worries about harms by strengthening the utilization process of the PHW to discourage tobacco use among users. We also feel that the additional provision in the proposed amendment of the COTPA bodes well for females who might be inclined to use tobacco. Raising the minimum age of sale of tobacco from 18 to 21 is likely to make a difference. Additionally when the ban on the sale of single cigarettes is implemented it will further discourage initiation especially among those who do not have much out of pocket money to spare for tobacco and that includes young females as well.

Expected results: All these provisions are likely to impact women as well. Studies show that if someone is not smoking by the time they are 21, there's only a 5% chance they will ever start smoking as an adult.

PD-919-28 Tobacco use and its correlates in slum communities of Kathmandu, Nepal

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Background: Slum communities are wide range of low-income settlements with inadequate living conditions and substandard facilities. They are among the most disadvantaged of the urban population. Tobacco use is one of the risky lifestyle behaviors in the urban slum communities of Nepal which has not been studied in detail. This study explores the prevalence of tobacco use and associated factors among urban slum population of Kathmandu Metropolitan City of Nepal.

Methods: A cross sectional survey was carried out in the four slum settlements of Kathmandu Metropolitan City in February 2015 using pre-tested questionnaire. A total of 300 households were selected randomly and the head of the household was interviewed. The χ^2 test and binary logistic regression were applied. Probability of significance was set at 5%. Participation in the study was voluntary and full confidentiality of the responses was maintained.

Results: Prevalence of tobacco smoking was 61.7% (females 64.3%, males 35.7%) and tobacco chewing was 31.7% (females 63.2%, males 36.8%). Nearly 60% of the respondents reported to have ever consumed alcohol and 6% had abused intravenous drugs. One fourth of the respondents believed that the current family income was insufficient to meet daily needs of the family. Multivariate analysis showed that tobacco smoking was significantly associated with ever consumption of alcohol (AOR = 4.6, 95%CI 2.6-8-14, $P < 0.001$).

Conclusion: Prevalence of tobacco use, both smoking and chewing, is high in the slum settlements of Kathmandu. Both forms of tobacco use were found to

be higher among the females. Poor families from the slums are more vulnerable to adoption of risky lifestyle behaviors like smoking, alcohol consumption and intravenous drug abuse. Comprehensive strategies are required in urban health policies to address high prevalence of tobacco use in urban slum communities.

PD-920-28 Evaluation of dual smoking (water pipe and cigarettes) and related factors in Iran

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Background: Dual use of tobacco products such as cigarettes and water pipe may be associated with increased risk of nicotine dependence and smoking-related complications. Accurate statistics are not available regarding the prevalence of water pipe smoking and particularly dual cigarette-water pipe smoking in the Iranian population. Thus, this study sought to assess the prevalence of dual cigarette/water pipe smoking and its related factors in Iran.

Methods: This cross-sectional study was conducted on Tehran residents >15 years of age selected via cluster, multi-stage randomized sampling from different geographical districts of Tehran in November and December 2014. The data were collected using the water pipe section of the Global Adult Tobacco Survey (GATS) questionnaire.

Results: A total of 1836 individuals participated in this study, of whom 243 (13.3%) were exclusive water pipe smokers, 76 (4.2%) were dual smokers of cigarettes and water pipe and 120 (6.6%) were exclusive cigarette smokers. Of dual smokers, 86.8% were males and 13.2% were females ($P < 0.001$). The mean age was 28.01 ± 8.7 year in exclusive water pipe smokers and 33.1 ± 1.1 years in dual smokers ($P < 0.001$).

Conclusion: The prevalence of dual smoking and exclusive water pipe smoking was 4.2% and 13.3%, respectively. Exclusive cigarette smoking had a prevalence of 6.1%. The frequency of dual smoking of cigarettes and water pipe was considerably high. High percentage of water pipe smoking indicates the public tendency to this habit. Dual smokers had a higher mean age than exclusive water pipe smokers and they were mostly males. The mean age at initiation of water pipe smoking in dual smokers was lower than the mean age at the onset of cigarette smoking. In other words, dual smokers started water pipe smoking sooner than cigarette smoking. Future studies with different methodologies are required to further scrutinize the relationship of water pipe and cigarette smoking. Smoking control programs must specifically target dual smokers.

PD-921-28 Factors associated with smoking among adult males in Colombo district, Sri Lanka

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Background: Although tobacco use begins primarily through the dynamic interplay of socio-demographic, environmental, personal and behavioral factors, a comprehensive model is better in assessing factors influencing smoking behavior. The PRECEDE model identify predisposing, enabling and reinforcing factors for initiating and maintaining smoking behaviors in order to assure appropriate intervention. The study was to determine the factors associated with smoking among males aged 20–59 years in Colombo District- Sri Lanka. **Methods:** A descriptive cross-sectional study was conducted with a representative sample of 1200 adult males selected using multistage cluster sampling in the District of Colombo. Information on smoking was assessed using an interviewer-administered questionnaire based on the PRECEDE model.

Results: Great majority of both ever smokers (66.6%) and never smokers (63.4%) had a good level of knowledge, 87.7% of ever smokers and 96.4% never smokers had unfavorable attitudes towards smoking. History of smoking by the father ($P < 0.001$), having a family member smoking in the presence of the respondent ($P = 0.004$), having close friends smoked regularly ($P < 0.001$) and getting frequently invitations to parties where friends regularly smoked when the respondent was young ($P < 0.001$) were found to be significant factors reinforcing the smoking habit. Ninety-two percent of the ever smokers have started smoking at the age between 20 to 30 years of age while 13.5% percent have bought the tobacco products as packets and 91.4% (540) have bought as single or multiple sticks at a time. Most of the ever smokers (93.7%) mentioned that there was a place to buy tobacco products near their house/school/work station when they were young. Majority could reach a shop to buy a tobacco product within 10 minutes.

Conclusion: The unfavorable attitudes on smoking is a predisposing factor for initiation and maintenance of smoking. Having a father and relatives who smoked, having friends who smoked and having frequent invitation for the parties when the participant was young were identified as the reinforcing factors while easy accessibility for tobacco products and frequent availability were identified as the enabling factors that were facilitated smoking behavior among the adult males of Sri Lanka.

PD-923-28 What drives youth towards tobacco use? Estimating predictors of tobacco use among youth in India: the GATS 2009–2010 Survey

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Background: Tobacco use among youth in India is affected by various sociodemographic factors, which form major predictors for its use. Focus on these predictors can help policy makers in curbing the large extent of morbidity and mortality due to tobacco. The present study was conducted to estimate the various socioeconomic factors associated with the tobacco use among youth.

Methods: This was a secondary data analysis of Global Adult Tobacco Survey, India 2009-2010, in the age group of 15-24 years. The predictors of smoking and smokeless tobacco use were analysed using data on occupation, education, and place of living among the youth. SPSS 17 was used for conducting the analysis.

Results: The youth (15-24 years) population in GATS 2009-10 was 13463. The total number of tobacco users (smokers and smokeless) among youth was 2969 (22.1%). There were 411 (3.1%) dual users. Smokeless form of tobacco (15.1%) was used more than smoked form among youth. Males and urban youth preferred smoked form of tobacco over smokeless form. Students took more of smokeless form of tobacco (OR 2.77, 95%CI 2.10–3.52). Smoking among youth had an inverse relation with increasing education level. Majority of tobacco users who use smokeless form and dual users belonged to poor socio-economic class.

Conclusion: This productive age group is more susceptible to tobacco addiction. The predictors of tobacco use among youth in this study varied in the group using smoked tobacco and smokeless tobacco. Hence policy makers need to differentially target youth who are males, from rural population, and with decreased level of education for smoked tobacco use; while poor class for smokeless tobacco use.

32. Second-line TB drugs: new drugs, new resistance, new challenges

PD-924-28 Performance of the MTBDRsl line probe assay for rapid detection of resistance to second-line anti-tuberculosis drugs and ethambutol in China

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Background: Extensively drug-resistant tuberculosis (XDR-TB) is a serious concern in China and new rapid detection method is urgently needed. This study was aimed to assess the performance of the GenoType MTBDRsl Line Probe Assay (LPA) for detection of resistance to levofloxacin (LFX), amikacin (AMK), capreomycin (CAP) and ethambutol (EMB) directly on sputum specimens at a national referral center in China. **Methods:** Smear positive sputum with multidrug-resistant tuberculosis (MDR-TB) identified by the GenoType MTBDRplus LPA were evaluated using the MTBDRsl LPA. The accuracy of the MTBDRsl test was assessed against phenotypic drug susceptibility testing (DST) as a reference, and sputum with discordant outcomes were assessed by gene sequencing.

Results: The interpretability of the MTBDRsl LPA was 96.8%. The sensitivity and specificity of the MTBDRsl test were 81.6% and 91.5% for LFX, 52.6% and 99.2% for AMK, 58.1% and 97.7% for CAP, 69.8% and 93.3% for EMB, and 56.1% and 100% for extensively drug-resistant tuberculosis (XDR-TB), respectively. The median turnaround time (TAT) was 3 days for MTBDRsl LPA compared to 85 days for culture-based DST, reducing the TAT by 96%. DNA sequencing revealed the mutation patterns in some of the isolates. 11/23 discordant LFX isolates had mutations in *gyrA* gene ($n=9$) and *gyrB* gene ($n=2$), 8/25 inconsistent EMB strains had mutations in *embB* gene, and 3/19 discordant AM isolates and 6/16 discordant CAP isolates had mutations in *rrs* gene, but none had mutation in *tlyA* gene.

Conclusions: The MTBDRsl LPA presents a specific screening tool to detect resistance to several key second-line anti-tuberculosis drugs and EMB in smear positive specimens. To further improve the test sensitivity, additional genetic mutations should be included.

PD-925-28 Genetic characterization of second-line drug-resistant and extensively drug-resistant *Mycobacterium tuberculosis* in North India

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Background: The increasing incidence of second line drug-resistant *Mycobacterium tuberculosis* in high-tuberculosis-burden countries further highlights the need for improved rapid diagnostic assays. Molecular diagnostic methods based on mutation detection are promising technologies for rapidly diagnosing DR-TB, but large studies of mutations in second line drug targeted genes as markers of resistance are rare. So this study was designed to analyze the Phenotypic and Genotypic Characterization of Second-Line Drug-Resistant and Extensively Drug-Resistant *Mycobacterium tuberculosis* from North Indian isolates.

Methods: A total 72 MDR-TB cases were screened for drug susceptibility testing for second line antibiotics i.e., ofloxacin, amikacin, kanamycin and capreomycin. Phenotypic drug susceptibility testing was performed using WHO recommended standard drug concentrations in BACTEC MGIT 960. Molecular characterization was done by DNA sequencing of *gyrA* gene for ofloxacin, and multi-allele specific PCR followed by PCR RFLP of *rrs* gene for second line injectable drugs (amikacin, kanamycin and capreomycin).

Results: Of the 72 MDR TB isolates, 16.7% (12/72) were extensively drug-resistant. Ofloxacin, amikacin, kanamycin and capreomycin resistance was detected in 54.2% (39/72), 37.2% (25/72), 30.5% (22/72) and 27.7% (20/72) cases, respectively. Cross resistance among second line injectable drugs was seen in 24 isolates, while 3 kanamycin and 2 capreomycin resistant isolates did not show cross resistance. Seven different types of mutations in QRDR region of *gyrA* gene were found in 92.2% (36/39) ofloxacin resistant isolates, most commonly in codons 94 (41%) and 90 (38.5%), while three did not have any mutation. The mutations in *rrs* gene were seen in 52% (13/25), 63.6% (14/22), 60% (12/20) isolates for kanamycin, amikacin and capreomycin resistant isolates, respectively.

Conclusions: The study characterized second line drug resistance associated mutations in *M. tuberculosis*. This information could be used for rapid screening of second line drug resistant TB.

PD-926-28 Susceptibilities of multidrug-resistant *Mycobacterium tuberculosis* culture isolates to unconventional drugs

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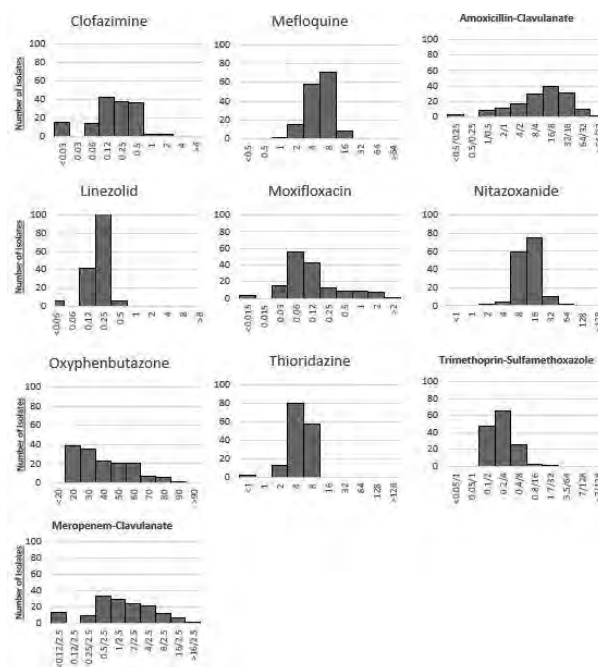
Background: The second-line agents currently recommended to treat drug-resistant tuberculosis (TB) are toxic, expensive, and often difficult to procure. As TB strains become increasingly resistant, the need for additional anti-TB drugs becomes more urgent. Drug development, however, takes time, and the resulting drugs are expensive. Some commercially available drugs have been reported to have anti-mycobacterial activity but are not routinely used because supporting laboratory and clinical evidence is sparse.

Methods: We used the resazurin microdilution assay to determine Minimum Inhibitory Concentrations (MICs) for trimethoprim-sulfamethoxazole (TMP-SMX), mefloquine (MEF), thioridazine (TDZ), clofazimine (CFZ), amoxicillin-clavulanate (AMX-CLV), meropenem-clavulanate (MPM-CLV), nitazoxanide (NTZ), linezolid (LZD) and oxyphenbutazone (OXY) against cultured isolates from sputum of TB patients with documented resistance to both isoniazid (INH) and rifampicin. INH and moxifloxacin (MOX) were used as a validation. We calculated the MIC₉₀ as the MIC at which 90% of isolates demonstrated no growth.

Results: Results from 217 isolates were analysed; 153 were from initial specimens from unique patients, and 64 were follow-up specimens from later in the course of treatment. Figure 1 shows the MIC frequencies for each drug; for compound agents, results are for the active agent. The MIC₉₀, in mcg/mL, against initial isolates were as follows: TMP-SMX = 0.4/8, MEF = 8, TDZ = 8, CFZ = 0.25, AMX-CLV = 32/16, MPM-CLV = 8/2.5, NTZ = 16, LZD = 0.25, OXY = 60. By comparison, the MIC₉₀ of INH was >4 and of MOX was 1.0, as expected.

Conclusions: Most agents demonstrated efficacy against *M. tuberculosis*. When these MICs are compared to the pharmacokinetic/pharmacodynamic profiles of the respective drugs in humans, TMP-SMX, MPM-CLV, LZD, CFZ, and NTZ appear particularly promising and warrant further clinical investigation.

Figure Histograms of MICs to isolates



PD-927-28 Validation of levofloxacin drug susceptibility testing in clinical isolates of *Mycobacterium tuberculosis*

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Background: WHO has recommended the use of later generation fluoroquinolones (FQs) such as levofloxacin (LVX) and moxifloxacin rather than older ones (ciprofloxacin) for the treatment of MDR patients. Therefore, it is important to establish susceptibility testing protocols for the newer FQs. This study is designed to validate the use of agar (7H10) proportion (AP) method for susceptibility testing of *M. tuberculosis* clinical isolates to levofloxacin replacing ciprofloxacin DST currently used in the laboratory.

Design/Methods: As a first step in the validation process, we chose the minimal inhibitory concentrations (MIC) method to determine the critical test concentration value of LVX for clinical strains of *M. tuberculosis* by using the standard AP method. A total of 102 strains selected from the culture collection of the National Reference Laboratory, Peru, were classified in 4 groups: I: strains ($n = 35$) from new patients (never received treatment) 'presumably sensitive' to FQs; II: strains ($n = 35$) from patients who failed treatment with first and/or second line drug regimens 'presumably resistant' to FQs; III: strains ($n = 17$) previously tested as ciprofloxacin (CIP) sensitive; and IV: previously tested CIP-resistant.

Results: The MIC of all susceptible strains including probable sensitive strains and CIP-sensitive strains (group I+III) was 0.25–0.5 µg/ml (51/52, 98%) and

1.0 µg/ml (1/52, 2%). On the other hand, MIC of all resistant strains which includes probable resistant strains and CIP-resistant strains (group II and IV) was ≥ 2 µg/ml for 68% of the strains (34/50) whereas 32% strains (16/50) had an MIC from 0.25–0.5 µg/ml.

Conclusions: Based on these MIC results, a concentration of 1.0 µg/ml is selected as the critical testing concentration. These results are in agreement with WHO recommended LVX critical concentration and published studies. MIC (0.25–0.5 µg/ml) below the critical concentration of resistant strains could be due to higher activity of LVX as compared to CIP. The critical concentration will be tested with a subset of pan-susceptible and resistant MTB strains for which MICs are near the critical values to verify that findings correlate with expected results and with specific mutations in the target genes.

PD-928-28 Evaluation of GenoType® MTBDRsl version 2 for detection of resistance to second-line anti-tuberculosis drugs in Ghana

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Background: TB control is challenged by the emergence of strains resistant to anti-TB drugs. Routine screening for drug resistance is essential for adequate case management and control. However, conventional procedures require elaborate infrastructure and expertise. Our objective was to evaluate the performance of line probe assay MTBDRsl version 2 (Hain Lifescience) for rapid screening of mycobacterial strains against second-line drugs.

Methods: We screened 117 (76 MDR, 14 RIF mono-resistant and 27 INH mono-resistant) resistant TB isolates against moxifloxacin (MOX), streptomycin (STR) and amikacin (AMK) using the Epsilometer test (E test). In addition, all the 76 MDR, 14 RIF^r and 3 INH^r were screened with the MTBDRsl. Resistant conferring genes, *gyrA*, *gyrB*, *eis*, *rrs*, *tap*, *whiB7* and *tlyA*, of strains resistant to MOX and or AMK were sequenced for mutation analysis.

Results: Isolates phenotypically resistant to STR, AMK and MOX were 38 (32.5%), 13 (11.1%) and 1 (0.9%), respectively. One MDR isolate was diagnosed as resistant to both MOX (MIC = 3 µg/mL) and AMK (MIC = 16 µg/mL) by both the phenotypic assay and MTBDRsl/LPA. Gene sequencing analysis led to the identification of *gyrA* (G87C) and *rrs* (A514C and A1401G) in this isolate. Whereas none of the remaining isolates were resistant to MOX (MIC < 0.125 µg/mL), 9/76 (11.8%) MDR, 1/14 (7.1%) RIF^r and 3/27 (11.1%) INH^r were resistant to AMK with MICs ranging from 1 to 8 µg/mL. However, the MTBDRsl/LPA identified none of these as resistant to AMK and only one MDR isolate among them harboured

a *tlyA* mutation (N236K). The agreement between the E-test and the LPA was 87.1% and 100% whereas the sensitivity/specificity was 7.7%/100% and 100%/100% for AMK and MOX respectively.

Conclusions: We report for the first time MDR-TB case that is also resistant to both a fluoroquinolone and a second line injectable in Ghana and also supports the use of the MTBDRsl version 2 for rapid detection of resistance to second line anti-TB drugs among MDR-TB cases. However, its inability to detect low-level resistance to AMK is a major concern.

PD-929-28 Development of an oligonucleotide array for detection of first- and second-line *Mycobacterium tuberculosis* drug resistance

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Background: Since conventional drug susceptibility testing (DST) has long turnaround time, rapid diagnosis of resistance is important for patients triage into different regimens. Drug-resistant tuberculosis (TB) is associated with mutations in several genes, including the *rpoB* gene for rifampin (RIF), the *katG* gene and the *inhA* regulatory region for isoniazid (INH), the *embB* gene for ethambutol (EMB), the *rpsL* and *rrs* genes for streptomycin (STR), *gyrA* and *gyrB* for fluoroquinolones, *rrs* and the promoter of *eis* for kanamycin (KM), amikacin (AM) and capreomycin (CM). We develop and evaluate a prototype oligonucleotide array for rapid detection of multidrug-resistant (MDR) and extensively drug-resistant (XDR) TB.

Methods: We selected 151 *M. tuberculosis* isolates with various DST profiles, including 137 multidrug-resistant, 6 RIF mono-resistant and 8 pan-susceptible isolates. The culture-based phenotypic DST was used as the gold standard. We designed 13 pairs of primers to amplify the aforementioned nine genes by a single multiplex PCR, and the digoxigenin-labeled amplicons were hybridization with probes immobilized on the array. After hybridization, alkaline phosphatase-conjugated anti-digoxigenin antibodies were used to reveal the hybridization signals. Besides, the GenoType MTBDRplus (GenoType) test and gene sequencing were performed to resolve the discordance between DST and the array.

Results: The detection limit of the prototype array was 250 pg per test. The sensitivities of the array for detecting RIF and INH resistance were 95.1% and 76.6%, respectively, whereas the sensitivities of the GenoType test for detecting RIF and INH resistance were 96.5% and 76.0%, respectively. No significant difference was found between the tests with respect to their sensitivities ($P = 0.25$). Moreover, the sensitivities for detecting EMB and STR resistance were 87.1% and 73.3%, respectively. For second-line drugs, the array displayed 90% sensitivity and 100% specificity in the detection of resistance to fluoroquinolones and the agreement with conventional DST was 95.4%. While for detecting KM/AM/CM

resistance, the array displayed 96-100% specificity, 61.1-88.9% sensitivity and the agreement with conventional DST was 92.1-98.7%. The turnaround time of the array was 6-7 hours.

Conclusion: The array can simultaneously detect MDR-/XDR-TB and directly reveal transmission-associated mutations, which is a powerful tool for clinical diagnosis and epidemiological investigations.

PD-930-28 In vitro activities of clofazimine in combination with ethambutol or bedaquiline against drug-resistant tuberculosis

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Background: To understand the synergistic effects of antituberculous drugs and to find efficacious combinations of molecules in order to improve the treatment outcomes of MDR-TB, we evaluated the in vitro activities of clofazimine (CFZ) in combination with ethambutol (EMB) or bedaquiline (BDQ) for the treatment of multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB).

Methods: We analyzed 49 *Mycobacterium tuberculosis* isolates of 36 MDR-TB and 13 XDR-TB cases. The minimum inhibitory concentrations (MICs) of single or combined CFZ, EMB and BDQ were determined using the established resazurin microtiter assay. The break-points of CFZ, EMB and BDQ are suggested to be 1.0 µg/mL, 5.0 µg/mL and 0.25 µg/mL, respectively. The fractional inhibitory concentration index (FICI) is calculated to interpret data as follows: FICI ≤ 0.5, synergy; 0.5 < FICI ≤ 2, indifference; and FICI > 2, antagonism.

Results: Among 36 MDR-TB isolates, the MICs distributions of CFZ alone and EMB alone were 0.06-1 µg/mL and 1-16 µg/mL, respectively. Compared with single drug, we observed respectively 1-4 fold decreases in CFZ MIC and 2-32 fold decreases in EMB MICs when administered in combination of CFZ and EMB except three MDR isolates. Moreover, among 13 XDR-TB isolates, the MICs distributions of CFZ alone and BDQ alone were 0.125-0.5 µg/mL and 0.03-0.12 µg/mL, respectively. Except one XDR isolate, in the combination of CFZ and BDQ, we observed respectively in 2-16 fold decreases in CFZ MICs and 1-2 fold decreases in BDQ MICs compared with single drug. Moreover, all of the 49 isolates were susceptible to CFZ, and all of the 13 XDR-TB isolates were susceptible to BDQ. In addition, 88.9% (16/18) MDR isolates which were initially resistant to EMB with MICs of ≥ 8 µg/mL became susceptible with MICs of ≤ 4 µg/mL when administered in combination with CFZ. When FICIs were calculated, we found only indifferent effects rather than synergistic or antagonistic effects in all tested isolates. The decreases of combined MICs of EMB might arise from the susceptibility of CFZ.

Conclusions: Our results suggest that CFZ is a suitable drug to combine with EMB or BDQ for MDR-/XDR-TB treatment.

PD-931-28 Performance of the new V2.0 of the GenoType® MTBDRs/ test

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Background: Detecting resistance to fluoroquinolones (FQ) and second-line injectable drugs (amikacin (AMK), kanamycin (KAN) and capreomycin (CAP)) is crucial given the worldwide increase in XDR-TB. A new version of the GenoType MTBDRs/ test (V2.0) has been developed to improve the diagnosis of resistance to FQ (involving *gyrA* and *gyrB* mutations) and resistance to second-line injectable drugs (involving *rrs* and *eis* promoter mutations) in *Mycobacterium tuberculosis*.

Methods: We performed a two phases study: 1) evaluating the performances of both the first (V1) and second (V2.0) version of the MTBDRs/ test on a collection of 127 multidrug-resistant (MDR) *M. tuberculosis* complex strains, and 2) evaluating the performances of the V2.0 prospectively in the laboratory workflow; using DNA sequencing and DST as comparators.

Results: The study comparing the performances of the MTBDRs/ V1 and V2.0 has shown that the specificities in resistance detection of both versions were similar, whereas the sensitivity of V2.0 was superior for FQ (94.8 vs. 89.6%) and KAN (90.5 vs. 59.5%), but similar for AMK (91.3%) and CAP (83.0%). Sensitivity and specificity of V2.0 were superior to those of V1 for the detection of pre-XDR (83.3 vs. 75.0% and 88.6 vs. 67.1%, respectively), whereas only the sensitivity of V2.0 was superior to that of V1 for the detection of XDR (83.0 vs. 49.1%). The study evaluating the V2.0's performances prospectively in the laboratory workflow is still ongoing.

Conclusions: MTBDRs/ V2.0 is superior to MTBDRs/ V1 and efficiently detects the most common mutations involved in resistance to FQ and aminoglycosides/CAP. However, due to mutations not recognized by V2.0 or resistance mechanisms not yet characterized (particularly mechanisms related to monoresistance to aminoglycosides or CAP), the results for strains detected as wild-type by MTBDRs/ V2.0 should be confirmed by further DNA sequencing and phenotypic drug susceptibility testing.

PD-932-28 Performance and utility of TaqMan Array Card for genotypic susceptibility testing for nine anti-tuberculosis drugs in MDR-TB

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Background: Phenotypic drug susceptibility testing is endorsed as the standard for second-line drug testing of *Mycobacterium tuberculosis* however it is slow and laborious.

Methods: We evaluated the accuracy of two faster and easier methodologies that provide results for multiple drugs: a genotypic TaqMan Array Card and the Sensititre MYCOTB plate. Both methods were tested at three central laboratories in Bangladesh, Tanzania, and Thailand with 212 MDR-TB isolates and compared with the laboratories' phenotypic method in use.

Results: The overall accuracy for ethambutol, streptomycin, amikacin, kanamycin, ofloxacin, and moxifloxacin vs. the phenotypic standard was 87% for TAC (range 70-99%) and 88% for the MYCOTB plate (range 76-98%). To adjudicate discordances we re-defined the standard as the consensus of the three methods, against which the TAC and MYCOTB plate yielded 94-95% accuracy while the phenotypic result yielded 93%. There were isolates with genotypic mutations and high MIC that were phenotypically susceptible, and isolates without mutations and low MIC that were phenotypically resistant, questioning the phenotypic standard.

Conclusions: In our view the TAC, MYCOTB plate, and the conventional phenotypic method perform similarly for second line drugs, however the former methods offer speed, throughput, and quantitative susceptibility information.

PD-933-28 Evaluation of diagnostic accuracy of Anyplex™ MTB/NTM/MDR-TB Detection with PrimeStore™ Transport Media, Thailand

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Background: Anyplex™ MTB/NTM/MDR-TB Detection is a molecular diagnostic test for simultaneous detection of *M. tuberculosis* complex and rifampicin and isoniazid resistance mutations. PrimeStore™ molecular transport media preserves and stabilizes mycobacterial DNA in sputum for up to 30 days without refrigeration, which is useful in settings requiring transport of samples to central laboratories. We evaluated the diagnostic perfor-

mance of Anyplex and PrimeStore technologies in two regions of Thailand.

Methods: We enrolled adults (≥ 18 years) who presented for care at five healthcare facilities if they had indications for TB culture and molecular testing according to national guidelines. Sputum was collected for MTBC culture, phenotypic drug-susceptibility testing (DST), and Anyplex testing on raw sputum and on sputum in PrimeStore transport media. We calculated test performance using culture as the gold standard including only those who were positive/negative for *M. tuberculosis* complex or drug resistance.

Results: From September 2014-June 2015, 813 enrolled patients had both sputum culture and Anyplex results available, of whom 154 (18.9%) were smear-positive. *M. tuberculosis* complex culture was positive in 204 (25.1%) patients. There were 269 (33.1%) patients who were positive for *M. tuberculosis* complex by Anyplex testing of raw sputum (sensitivity 91%, specificity 85%); 272 patients (33.5%) were positive by Anyplex testing of sputum in PrimeStore (sensitivity 88%, specificity 84%; Table). 182 of 204 *M. tuberculosis* complex culture-positive patients had DST results; 18 (9.9%) and 33 (18.1%) isolates exhibited phenotypic rifampicin and isoniazid resistance, respectively. Anyplex on raw sputum identified 21 patients with rifampicin-resistant tuberculosis (sensitivity 94%, specificity 97% when compared to DST) and 29 patients with isoniazid-resistant tuberculosis (sensitivity 88%, specificity 99%). Anyplex with PrimeStore identified 19 patients with rifampicin-resistant tuberculosis (sensitivity 94%, specificity 98%) and 26 with isoniazid resistance (sensitivity 83%, specificity 99%).

Conclusions: Anyplex, with or without PrimeStore, had higher sensitivity but substantially lower specificity than previously reported in laboratory-based evaluations. Possible reasons for lower specificity of Anyplex for *M. tuberculosis* complex include erroneously negative cultures, some patients already were on treatment (thus Anyplex detected *M. tuberculosis* complex DNA, but cultures did not detect viable mycobacteria), or incorrect Anyplex results due to cross-contamination during molecular testing.

Table Test performance of Anyplex™ MTB/NTM/MDR-TB Detection

	Anyplex™ + raw sputum	Anyplex™ + PrimeStore™	Anyplex™ + raw sputum	Anyplex™ + PrimeStore™
	Sensitivity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)	Specificity (95% CI)
Diagnose MTBC	91% (87-95%)	88% (83-92%)	85% (83-88%)	84% (81-87%)
Diagnose RIF-R	94% (84-100%)	94% (83-105%)	97% (95-100%)	98% (96-100%)
Diagnose INH-R	88% (76-99%)	83% (69-97%)	99% (98-100%)	99% (97-100%)

PD-934-28 Use of fosfomycin to control contamination of *Mycobacterium tuberculosis* culture in the BD BACTEC™ MGIT™ 960 System

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Background: The BD BACTEC MGIT 960 System is widely used for rapid and efficient mycobacteria recovery but high contamination rates threaten its diagnostic performance. Aggressive decontamination removes contaminants, but may also affect growth of *M. tuberculosis*. Other techniques facilitate growth of both *M. tuberculosis* and contaminants. Fosfomycin is active against many gram-negative and -positive bacteria responsible for culture contamination but inactive against *M. tuberculosis*. We evaluated the introduction of fosfomycin as a selective agent in BACTEC MGIT 960 culture for *M. tuberculosis*.

Methods: Fosfomycin was added to MGIT 960 cultures performed between February and April, 2015 in the SES Lab- Lima Peru. Sputum samples tested were collected from patients with pulmonary TB either at diagnosis or during follow-up. Each sample was divided into two aliquots for inoculation: 1) MGIT tube (reference) and 2) MGIT tube + 1 ug of fosfomycin. To assess the role of fosfomycin as a selective agent in MGIT culture, we compared the frequency of positive and contaminated *M. tuberculosis* cultures in the paired samples. Moreover, to assess the effect of fosfomycin on MTB growth, we compared the time to positivity (TTP) and colony forming units (CFU) in MGIT cultures in the presence or absence of fosfomycin. The comparison of results were performed by Student's *t* test, Wilcoxon signed-rank test and Mc Nemar test (significance values of $P < 0.05$).

Results: 62 sputum samples from patients with pulmonary TB were included. Volume and appearance in specimens was no significantly different between positive, negative and contaminated cultures. In cultures treated with fosfomycin, *M. tuberculosis* was recovered (45/62) more frequently than reference cultures (35/62; $P = 0.002$). Contamination was less frequent with fosfomycin than in the reference (2/62 vs. 12/62; $P < 0.001$). CFU counts and time to positivity (TTP) were not different between cultures with and without fosfomycin ($P = 0.617$; $P = 0.576$, respectively. Table.)

Conclusions: The addition of fosfomycin may be an effective alternative for control of contamination in BACTEC cultures without significantly interfering with growth of *M. tuberculosis*. In addition, it is inexpensive, which could facilitate its introduction in labs in resource-limited settings.

Table Fosfomycin influence on BACTEC MGIT 960 cultures

Result	MGIT culture without fosfomycin n/N	MGIT culture with fosfomycin n/N	P value
MTB positive cultures (%)	35/62 (56.5)	45/62 (72.6)	0.002 (McNemar test)
Contaminated cultures (%)	12/62 (19.4)	2/62 (3.2)	<0.001 (McNemar test)
Time to positivity in hours (mean \pm SD)	363.9 \pm 193.6	359.9 \pm 173.4	0.576 (Student's <i>t</i> -test for related samples)
cfu counts per ml (mean \pm SD)	184.2 \pm 105.7	176.6 \pm 101.4	0.617 (Wilcoxon signed-rank test)

33. Expanding the diagnostic landscape: looking beyond sputum samples

PD-935-28 Comparison of five methods for recovery of *Mycobacterium tuberculosis* DNA from stool samples

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Background: Laboratory diagnosis of pulmonary tuberculosis is based on sputum, but in patients who cannot produce sputum (i.e., children), invasive procedures, such as gastric aspiration, may be used to obtain alternative specimens. Non-invasive samples, such as stool, are an attractive alternative for diagnosis; however, the presence of many inhibitors presents a challenge for molecular testing. We compared five *M. tuberculosis* DNA extraction methods to determine which method maximizes DNA recovery while minimizing the presence of PCR inhibitors.

Methods: Healthy volunteer participants provided stool samples, which were divided, allowing each extraction method to be run on two aliquots per volunteer. Stool aliquots were inoculated with high (10 cells/mg) and low (1 cell/mg) bacterial suspensions. Positive, negative and system controls were used in each procedure. Samples were submitted to five DNA extraction methods, with corresponding sample mass: QIAamp DNA Stool Mini Kit QIAGEN (0.3g), QIAamp DNA Stool Mini Kit Qiagen with Microsens TB-Beads (5g), PowerFecal DNA Isolation Kit MO BIO Laboratories (0.3g), Akonni Biosystems automated TruTip Kit (5g), and Akonni TruTip with Microsens TB-Beads (5g). Isolated *M. tuberculosis* DNA was amplified using a real-time PCR assay specific for *M. tuberculosis* complex (IS6110 targeted). Ten-fold dilutions of the high concentration extracts were amplified and compared to the undiluted sample to quantitate percent inhibition.

Results: Seventy-one stool aliquots underwent DNA extraction, including controls. Real-time PCR results showed the following average CPs for high and low bacterial suspensions, respectively: QIAGEN Kit (32.6 and 33.3), Qiagen Kit with Microsens Beads (32.7 and 33.8), PowerFecal Kit (30.7 and 31.3), Akonni TruTip (31.7 and 33.8) and Akonni TruTip with Microsens Beads (31.9 and 33.7). The average percent inhibition was 52% for PowerFecal, 52% for Akonni TruTip, 31% for Akonni TruTip with Microsens TB-Beads (4/5 dilutions detected), and 54% for Qiagen Kit with Microsens beads (2/4 dilutions detected). Diluted samples from Qiagen Kit extracts did not amplify.

Conclusions: PowerFecal DNA Isolation Kit, followed by Akonni TruTip, showed the best DNA recovery from healthy patients' stool samples inoculated with bacterial suspensions of *M. tuberculosis*. These kits could be a good alternative to purify DNA and need to validate its use with TB diagnosis molecular methods.

PD-936-28 Xpert® MTB/RIF assay for detection of *Mycobacterium tuberculosis* in stool samples of patients with pulmonary tuberculosis

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Background: The Xpert MTB/RIF (Xpert) technology allows rapid and sensitive diagnosis of pulmonary tuberculosis (TB) in sputum specimens. However, diagnosis of pulmonary TB (PTB) is difficult for patients who cannot produce sputum, a problem that is particularly common in young children, human immunodeficiency virus-positive and elderly patients. The objective of this study was to investigate the use of Xpert assay for successful detection of PTB using stool samples from adult subjects.

Methods: The study was conducted between the periods of December 2012 to September 2013. Stool and sputum samples from known smear positive PTB patients were collected from a TB Hospital in Dhaka and considered as 'case'. Stool samples were also collected from non-TB healthy individuals from a slum area of Dhaka and considered as 'control'. Stool and sputum samples were decontaminated and concentrated using NALC-NaOH-Na-citrate solution and the resultant sediment was used for Xpert assay, acid-fast bacilli (AFB) microscopy and culture. The results of Xpert assay, AFB microscopy and culture using stool and sputum specimens were compared.

Results: A total of 103 stool samples were collected from cases and another 50 stool samples from controls. Xpert assay detected *M. tuberculosis* in 92 (89.3%) of 103 stool samples from sputum smear microscopy positive cases, whereas all 50 stool samples from healthy controls were negative by the assay. Among 54 sputum culture positive cases, 50 (92.6%) were detected by Xpert assay in stool.

The load of *M. tuberculosis* in stool samples detected by Xpert assay found high with increasing grade of stool AFB microscopy. Moreover, stool Xpert had 100% agreement with the results of sputum Xpert and culture for detection of rifampicin susceptibility.

Conclusions: The present study demonstrates that the Xpert assay on stool samples might be very useful for the diagnosis of PTB. Although the assay has been standardized using stool samples from adult subjects, the optimized protocol of stool processing for Xpert assay would be beneficial for those patients who cannot produce sputum for the diagnosis of PTB including the children.

PD-937-28 Application of a quantifiable stool RT-PCR assay to increase diagnostic yield in childhood TB

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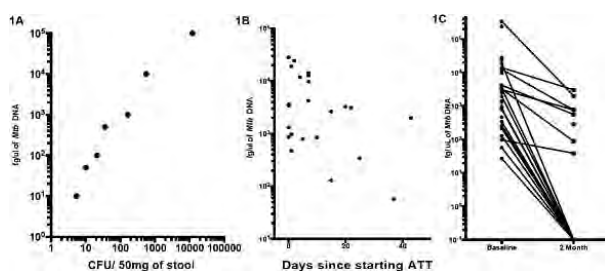
Background: Quantification of *Mycobacterium tuberculosis* has potential to improve TB diagnostics and treatment monitoring, with particular relevance in childhood TB as its paucibacillary nature presents a diagnostic challenge. We evaluated the diagnostic yield of quantitative real-time PCR for the detection of *M. tuberculosis* in stool.

Methods: Stool was collected from a cohort of adults and children with confirmed or clinically diagnosed TB ($n = 67$). DNA was isolated from 50 mg of stool using the MP Fast DNA soil kit. Tuberculosis-specific primers were designed from the IS6110 insertion element found exclusively within the *M. tuberculosis* complex. To determine a limit of detection (LOD), 10 to 10⁶ CFU of H37 Rv *M. tuberculosis* was spiked into 50 mg of healthy stool and the DNA was isolated. All samples were analyzed using quantitative real-time PCR.

Results: The LOD of *M. tuberculosis* was < 10 CFU of *M. tuberculosis* per 50 mg of stool. The CFU of *M. tuberculosis* spiked into stool and DNA quantified by PCR was well correlated (Figure 1A Spearman $r = 0.998$, $P < 0.0001$). The quantity of *M. tuberculosis* DNA detected inversely correlated with time on ATT (Figure 1B; Spearman $r = -0.4219$; $P = 0.04$). The quantified *M. tuberculosis* DNA in stool at 2 months was lower than baseline levels (Figure 1C, Wilcoxon signed rank test; $P < 0.0001$). Stool qPCR had similar diagnostic accuracy as sputum GeneXpert MYB/RIF (Xpert) amongst individuals who had stool collected within 72 hours of ATT initiation (Fisher's exact $P = 0.32$). Stool PCR identified 15% (4 of 26) children who were clinically diagnosed with TB despite having negative Xpert and culture results.

Conclusions: Detection of *M. tuberculosis* DNA from stool provides a quantifiable measure of an individual's *M. tuberculosis* burden. PCR detection of *M. tuberculosis* in stool of children with clinically diagnosed TB (Xpert and culture negative) highlights the potential for this assay to increase bacteriologic confirmation of childhood TB.

Figure Quantification of *M. tuberculosis* in stool



PD-938-28 Experience in applying the Xpert® MTB/RIF assay to diagnose bone and joint tuberculosis in Uzbekistan

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Background: Effective and rapid microbiological diagnostics of extra-pulmonary tuberculosis (TB) is currently a highly relevant topic. Difficulties in detecting a TB pathogen in patients with bone and joint TB (BJTB) result in misdiagnoses and prescription of incorrect treatment regimens. Traditional test methods on the market such as smear microscopy and culture tests are labour-intensive and time-consuming for *Mycobacterium tuberculosis* detection in bone material. The introduction of GeneXpert® MTB/RIF assay into the TB control service of Uzbekistan enhanced test quality and reduced time of *M. tuberculosis* detection in bone material.

Methods: The study was conducted at the National Reference Laboratory. Diagnostic material consisted of 52 bone samples collected from patients with presumptive BJTB. All samples were decontaminated using NALC-NaOH method and subsequently inoculated into Löwenstein-Jensen and MGIT Middlebrook 7H9 media. Molecular genetic tests were performed on processed sediment using multiplex amplification technology of Xpert.

Results: The polymerase chain reaction (PCR) analyzer of Xpert enabled identification of DNA of *M. tuberculosis* pathogen in 28 (54%) patients. Among positive results, resistance to anti-TB drug, Rifampicin, was found in 8 (28.5%), sensitivity was detected in 19 (68%) cases, while in 1 patient (3.5%), Rif resistance was indeterminate. Test error rate was 1 (2%) case.

Unlike smear microscopy and culture methods, Xpert assay was more sensitive in detecting *M. tuberculosis* in bone material. Smear microscopy detected acid-fast bacteria in 8 (15%) patients. In 28 (54%) patients with positive Xpert results, 14 (50%) cultures showed growth on MGIT Middlebrook 7H9 medium and 11 (39%) on Löwenstein-Jensen medium.

Conclusions: Xpert MTB/RIF is considerably more sensitive than smear microscopy and culture methods in laboratory investigation of bone material for BJTB cases. Xpert may be used as an initial diagnostic test when verifying diagnosis in possible BJTB cases to facilitate the start of timely and adequate treatment.

PD-939-28 Rapid detection of multidrug resistance in *Mycobacterium tuberculosis* from direct smear-negative sputum samples by high-resolution melt curve analysis

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Background: Drug-resistant TB is a major threat for TB control worldwide and WHO estimates that 59% of reported TB patients estimated to have MDR-TB were not detected in 2014. India holds the dubious distinction of harboring 23% of the global TB burden with 2.2% of its new TB cases and 20% of previously treated cases having MDR-TB. This study was carried out to evaluate high resolution melt curve analysis (HRM) for the rapid detection of multidrug resistance in *Mycobacterium tuberculosis* in India.

Methods: We designed a plasmid library of most common mutations of resistance determining regions of *rpoB*, *katG* and *inhA* promoter and used them as positive controls in the HRM assay. The HRM assay was first evaluated with 100% concordance in a known set of 25 MDR *M. tuberculosis* clinical isolates. Final validation was carried on DNA isolated from 99 *M. tuberculosis* culture positive sputum samples (including 68 sputum smear negative, culture positive patients, SSM-/C+) to assess their MDR status (RIF and/or INH resistance). DNA sequencing was used as the gold standard.

Results: We were able to discriminate the mutant samples from wild type by analyzing the melting-curve patterns through the HRM software in all 99 sputum specimens. The genotype of the various patterns could be identified due to the control plasmids put along with the assay. In our study, RIF monoresistance was 11%, INH monoresistance was 21% and 5% of the patients had MDR-TB. Sensitivity of HRM assays for detection of RIF and INH resistance were 84.6% (*rpoB*), 86.4% (*katG*) and 100% (*inhA*), with 100% specificity. The concordance between sequencing and HRM assay was 97%. HRM assay was able to detect mutations in heteroresistant samples also which were some time undetectable by DNA sequencing.

Conclusions: HRM assay offers the advantage of a rapid, cost effective, closed-tube and single step rapid screening method for detection of MDR TB.

PD-940-28 Utility of the Myco/F lytic culture system for recovery of *Mycobacterium tuberculosis* from sterile body fluids

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Background: The diagnosis of extrapulmonary tuberculosis (EPTB) is challenging due to limitations in sampling from the affected sites and the paucibacillary nature of the specimens. Rich culture media are generally more sensitive in detecting *M. tuberculosis* in sputum and other clinical samples. This study evaluated the performance of Myco/F lytic culture system for recovery of *M. tuberculosis* in extrapulmonary specimens.

Methods: A total of 209 samples, including 104 pleural fluid, 74 pus, 14 cerebrospinal fluid and 17 bone and joint biopsy, were collected from patients suspected to have EPTB and tested by ZN smear microscopy, Löwenstein-Jensen (LJ) culture MGIT 960 culture and Myco/F lytic liquid culture.

Results: Using clinical diagnosis as reference, the sensitivity of Myco/F lytic system, MGIT960 system, LJ culture and smear in tuberculous pleurisy diagnosis was 33.33% (34/102), 24.51% (25/102), 12.75% (13/102) and 3.92% (4/102), respectively, in bone and joint tuberculosis diagnosis was 67.86% (57/84), 59.52% (50/84), 36.90% (31/84) and 33.33% (28/84), respectively, and in tuberculous meningitis diagnosis was 6.25% (1/16), 6.25% (1/16), 6.25% (1/16) and 0% (0/16), respectively, and the specificity values of all these assay was 100%. The specificities and sensitivities of the Myco/F lytic system for the recovery of *M. tuberculosis* from sterile body fluids (pleural fluid, pus and CSF) are not statistically different than those of the MGIT960 system. For pleural fluid samples, the time to positivity was significantly shorter in the MGIT culture vs. that in the Myco/F lytic liquid culture (17.10 days vs. 25.26 days), respectively ($P = 0.009$). For pus samples, the time to positivity was 23.11 days and 24.19 days for MGIT culture and Myco/F lytic liquid culture, respectively ($P = 0.73$).

Conclusions: The Myco/F lytic culture system may be an alternative to the MGIT system for diagnosing EPTB using sterile body fluid samples.

PD-941-28 Comparative performance of the Loopamp™ MTBC Detection kit for rapid detection of complex *Mycobacterium tuberculosis*: a retrospective study

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Background: Despite the availability of highly efficacious treatments for decades, tuberculosis remains a major public health problem worldwide. Early and accurate diagnosis is important for the control and prevention of the disease. Nucleic acid amplification tests (NAATs) are commonly used in industrialized countries for quick and specific detection of *Mycobacterium tuberculosis* complex (MTBC) in clinical specimens but its implementation is limited in resource limited countries. Recently, a NAAT commercial assay, Loopamp™ MTBC detection kit (Eiken, Japan), was developed for diagnosis of pulmonary tuberculosis in microscopy centers. In this study we aim to evaluate the performance of Loopamp MTBC detection kit on frozen sputum samples of suspected TB patients, by comparing with Xpert® MTB/RIF assay.

Methods: This study was conducted between 2013 and 2014 at the Institut Pasteur in Cambodia (IPC), Phnom Penh, Cambodia. The performance of Loopamp MTBC detection kit and Xpert MTB/RIF test for the detection of MTBC DNA were compared by use of 196 frozen sputum specimens (81 smear- and culture-positive, 16 smear-negative and culture-positive and 99 smear- and culture-negative). The specimen were collected between 2010 and 2013 from sample received as part of routine TB diagnostic activity of the Mycobacteriology Laboratory of IPC.

Results: The Loopamp MTBC assay and Xpert MTB/RIF were highly specific and exhibited excellent sensitivity (100%) with smear-positive specimens. Both methods exhibited similar sensitivities with smear-negative specimens (56.3% Loopamp MTBC and 43.8% for Xpert MTB/RIF). The overall sensitivities of the Loopamp MTBC and Xpert MTB/RIF assay were 92.8% (95%CI 85.8–97) and 90.7% (95%CI 83.1–95.7), respectively. The overall performance of Loopamp MTBC and Xpert MTB/RIF assay is significantly higher than that of FM ($P < 0.05$).

Conclusions: Loopamp MTBC assay is a simple rapid nucleic acid amplification method and well adapted to a routine TB laboratory. It appears to be as sensitive and specific as Xpert MTB/RIF assay in the detection of MTBC in sputum sample.

PD-942-28 Usefulness of a loop-mediated isothermal amplification (LAMP) test for diagnosing pulmonary tuberculosis in a clinical setting

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Background: Early case detection of pulmonary TB is the key to accelerating a decline in incidence in the era of the End TB Strategy. Loop-mediated isothermal amplification (LAMP) is a simple nucleic acid amplification method that does not require expensive devices or computerized-detection systems.

Objective: To examine the usefulness of a LAMP test (TB-LAMP, Eiken Chemical Co Ltd) for diagnosing pulmonary TB in a clinical setting by comparing smear and culture examination.

Methods: We compared the performance of LAMP test with that of smear microscopy and culture (MGIT and LJ method) at a tertiary hospital in China, examining one of the three sputum specimens collected from hospitalized presumptive TB cases together with other routine medical examinations.

Results: 317 presumptive TB cases in May-Sept, 2015 were analyzed. There were 78 (25%) smear-positive cases, of which 74 (95%) were LAMP-positive, 72 (92%) were MGIT-positive, and 65 (83%) were LJ-positive. Of the 239 smear-negative cases, LAMP test showed a higher positivity rate than MGIT (81 (34%) vs. 69 (29%), $P = 0.0744$) and LJ (81 (34%) vs. 62 (26%), $P = 0.0061$). The combined culture positivity rate (MGIT or LJ) among the smear-negative cases was 34%. Among the 78 smear-positive cases, the sensitivity and specificity for positive culture (MGIT or LJ) was 99% (95% confidence interval (CI): 92-100%) and 60% (95%CI 17-93%), respectively. Among the 239 smear-negative cases, the sensitivity and specificity for positive culture was 78% (95%CI 67-86%) and 89% (95%CI 82-93%), respectively.

Discussion: At present study, LAMP test showed the similar positivity rate to culture examination; by using LAMP test, twofold bacteriologically positive TB cases were detected than by smear microscopy within an hour. Culture examination doesn't always become gold-standard in practical settings because it sometimes shows a false-negative test result by too harsh decontamination. Most of the LAMP-positive, culture-negative cases in the study were clinically diagnosed as active TB, based on CT scan and anti-TB treatment response.

Conclusion: LAMP test is comparable in the positivity to culture examination in actual medical practices. Further case-by-case analysis on the discrepant results between LAMP test and culture needs to be made.

PD-943-28 A novel bead-based extraction method for improved qPCR and next-generation sequencing of *Mycobacterium tuberculosis* from low target samples

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Background: Quantitative PCR (qPCR) and next-generation sequencing (NGS) are established molecular methods that continue to improve detection and genetic characterization of *Mycobacterium tuberculosis* (MTB). However, these nucleic-acid based approaches are limited by the initial concentration and purity of the RNA/DNA from collected specimens. PrimeStore MTM[®] (PS-MTM) is a specimen collection and transport medium that inactivates MTB and preserves nucleic acid at elevated temperature for downstream qPCR and NGS. **Aim:** A bead-based extraction employing optimized buffers and chemically coated magnetized beads for concentrating and subsequently purifying nucleic acids from samples was developed to enhance qPCR and NGS from low-level samples.

Methods: Ten-fold serial dilutions of MTB (10^5 to 0.1 CFU/mL) were prepared in PS-MTM and detected and genetically characterized using an ABI-7500 instrument and Illumina MiSeq, respectively. Prior to amplification/sequencing triplicate nucleic acid extractions were performed for each dilution using bead-based extraction and compared to equivalent extraction performed using Qiagen.

Results: According to qPCR, bead-based extraction was more sensitive, i.e., lower cycle threshold (CT) values at each MTB dilution. At the lowest 0.1 CFU/mL dilution, MTB was detected (Avg $C_T = 32.6$; S.E. = 0.2) using bead-based extraction but not detected ($C_T = 40$) from extractions using Qiagen. Furthermore, NGS yields including total reads and coverage were improved using bead-based nucleic acid extraction compared to yields obtained using Qiagen extraction.

Conclusions: This novel bead-based method includes a concentrating step that provides a ten-fold improved increase in total nucleic acid concentration compared to standard Qiagen extraction. Magnetized beads and optimized chemistry produce cleaner extraction preparations that result high purity RNA/DNA from a wide range of clinical matrices including sputum. Enhanced DNA isolation, particularly from low-level smear-negative sputum will increase MTB positives using qPCR and enhance NGS performance. This methodology may be important for improving qPCR detection and next-generation sequencing of pathogens directly from low target clinical specimens.

PD-944-28 Predicting mycobacterial load from the time of positive culture using the microscopic-observation drug-susceptibility assay

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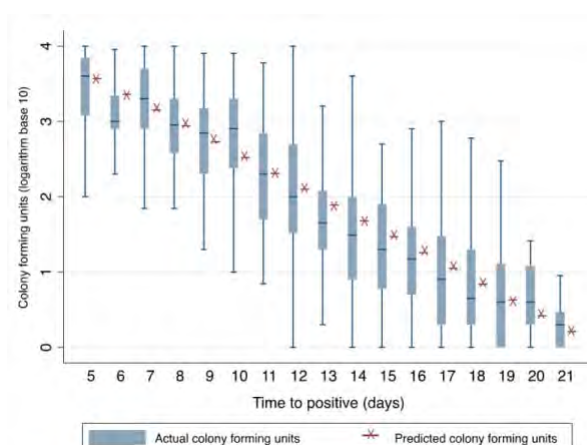
Background: MODS (microscopic-observation drug-susceptibility assay) is a rapid, non-commercial method to culture *Mycobacterium tuberculosis* using 7H9 broth media, which can also identify drug sensitivity directly from sputum samples and it has been endorsed by the World Health Organization. To assess mycobacterial load in sputum with MODS, colony forming units (CFU) are counted, however this is a complex process, therefore our objective was to assess the role of time to positive culture (TTP) data to predict the number of CFU in MODS cultures.

Methods: Fresh sputum samples were collected from tuberculosis-affected persons in Ventanilla, Lima, Peru. Samples were processed by the standard MODS protocol with biosafety precautions. MODS cultures were read 3 times a week from 5 days until 21 days after inoculation. The TTP was calculated as the days taken for the first colony to appear in the MODS culture, and CFU was the number of colonies seen the last day of culture. Linear regression analysis was used to predict CFU from the TTP of the same sample.

Results: During the study period there were 1934 samples positive for *M. tuberculosis* in MODS. The median TTP was 11 days (interquartile range, IQR 8-14), and median CFU 2.2 (IQR 1.3-3.1). There was a strong inverse correlation between TTP and CFU, that for every 4.8 (95% confidence interval 4.5-5.0) days needed in TTP there was a 10-fold decrease in CFU ($R^2=0.63$, $P < 0.0001$). Using this simple linear regression model, figure compares the actual CFU data with the predicted value from paired TTP data. 86% of actual CFU values were within 1 base-10 logarithm of the predicted CFU values.

Conclusions: We conclude that TTP culture data can be used as a surrogate marker for CFU. Calculating TTP is a simple and feasible technique for evaluating mycobacterial load in sputum.

Figure Actual CFU vs. predicted value



34. Prisons: the smoking gun

PD-945-28 Profile of tuberculosis patients in prisons in Japan: a cross-sectional study

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Background: Characteristics of TB prisoner patients in Japan are not well understood and little has been reported publicly.

Objective and Methods: We conducted a cross-sectional study whereby clinical records of TB patients who were treated at one prison institution between 2009 and 2014 were reviewed. Where possible, comparison with the general prison population was made. Proportions were compared using a χ^2 test. Kaplan-Meier survival analysis was also conducted to determine the time from entry to prison institution to diagnosis of TB. All analysis was performed using R 3.1.3. The study protocol was approved by the ethics committee of the Research Institute of Tuberculosis, and the Japanese Association of Correctional Medicine.

Results: Between 2009 and 2014, a total of 49 TB patients received treatment. 69.4% were males and 95.4% were Japanese. Of the 49 TB patients, 43 had pulmonary TB (PTB), 4 had extra-pulmonary TB (EPTB) and 2 had concomitant PTB and EPTB. Of the 45 PTB cases, 71.1% were smear positive, and 71.1% were culture-confirmed. There were no multi-drug resistant TB, however, the results of drug sensitivity test were unknown for 19.4% of the culture confirmed cases. The proportion of unemployed, and those without permanent address prior to incarceration, and proportion of those with psychological disorder among the prisoner TB patients were significantly higher than that of the general prison population (83.7% vs. 31.5%, 42.9% vs. 19.3%, 9.7% vs. 1.8%, $P < 0.001$). The median time to

diagnosis since time of entry to prison institution was 134 days (95% confidence interval: 67-373).

Conclusion: Poor socio-economic status prior to incarceration, and psychological disorder were indicated as potential risk factors for TB among prisoner population. Also considering the relatively short time between entry to prison and diagnosis, our results suggest that prisoner TB patients were more likely to be infected prior to entering prison and develop the disease while being incarcerated.

PD-946-28 Factors associated with poor treatment outcomes of MDR-TB treatment in Tomsk penitentiary system in Russia among patients enrolled during 2000–2009

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Background: Treatment of MDR-TB in Tomsk Oblast prisons in Russia started as a pilot project in September 2000. Since then more than 600 prisoners have been treated according to international standards.

Methods: The objective of the research was to assess the results of treatment and factors associated with different outcomes. We analyzed a cohort of patients with bacteriologically confirmed multidrug-resistant tuberculosis (MDR-TB) who started treatment in Tomsk penitentiary system between September 2000 and April 2009. Treatment outcomes were defined as ‘successful’ (cured and treatment completed), ‘unsuccessful’ (failure, died) and ‘lost to follow-up’. We used univariate (χ^2 and student’s *t*-test) and multivariate logistic regression models in our analyses.

Results: We enrolled 477 patients with confirmed MDR-TB, of whom 367 (77%) had successful outcome, 45 (10%) had unsuccessful (8% failed; 2% died), and 65 (13%) were lost to follow up. In the multivariate analyses unsuccessful treatment was significantly associated with the presence of diabetes mellitus (OR=14.8, *P* = 0.007), XDR-TB (OR=10.8, *P* < 0.001), bilateral cavitory disease on chest X-Ray (OR = 3.7, *P* = 0.002), history of hemoptysis (OR = 3.1, *P* = 0.043) and positive smear at the start of treatment (OR = 2.2, *P* = 0.045). The following risks were associated with lost to follow up outcome: release from prison during therapy (OR = 3.5, *P* < 0.001) and longer than 2 years history of TB (OR = 2.1, *P* = 0.021).

Conclusions: Patients with identified risk factors should be closely monitored throughout treatment. Management of diabetes mellitus, access to surgery, stronger treatment regimens, aggressive treatment of side effects, and adherence-improving approaches for patients after release from prisons are essential to ensure better treatment outcomes.

PD-947-28 Prevalence and risk factors associated with latent tuberculosis infection in security guards from a Colombian prison

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Background: The prisons are considered a reservoir for TB. We wanted to determine the prevalence of latent tuberculosis infection (LTBI) in security guards and to identify risk factors associated with it.

Methods: In a previous study we found a high prevalence and incidence of LTBI in prisoners in two Colombian prisons (77.6% and 29%, respectively). Now, we conducted a cross-sectional study in security guards from one prison in Medellín, Colombia. They were included if: agreed to participate in the study and signed the consent form and they were excluded if: prior or active tuberculosis (TB); prior Tuberculin Skin Test (TST) administration; immunosuppressive treatment; and administration of live vaccines (MMR, varicella or LAIV) in the 4 weeks before TST application. The TST was administered according to CDC guidelines. Reading was conducted within 48 to 72 hours of administration. A positive TST result was considered as an induration of ≥ 10 mm diameter for non-HIV infected people, and ≥ 5 mm for HIV-infected subjects. If the first TST result was negative, the TST was repeated in 2-3 weeks. Bivariate and multivariate analysis was done, expressing Prevalence Ratio (PR) with 95% confidence interval.

Results: The overall prevalence of LTBI by two-step method was 46.3%. In the first TST administration 27.8% guards were positives, and the second TST an additional 18.5%. The median age was 29 years, and hours inside of prison per day was 24 hr. History of contact with active TB case was related in 80% (95% were inmates). The percentage of BCG scar was 88%, past history of smoking was elicited in 28%. Security activities was documented in 64%, the other 36% carry out administrative work. The past history of smoking was a risk factor associated with a positive TST (RP = 1.07; 95%CI 1.8-1.9).

Conclusions: The prevalence of TST in security guards was high. The contact with inmates with active TB may be contributing to the prevalence observed in this population.

PD-948-28 A linked epidemic? Incarcerated populations may drive tuberculosis rates in the general population

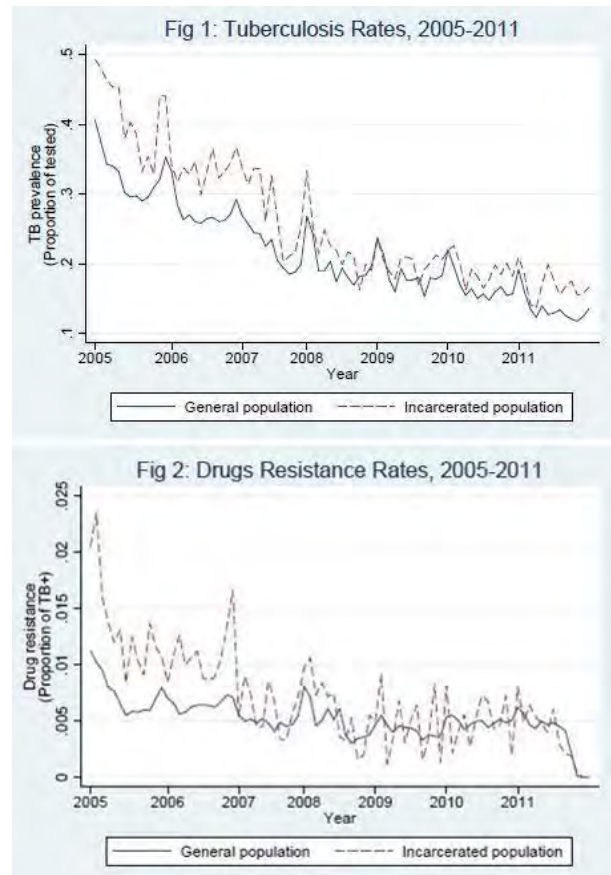
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Background: Tuberculosis (TB) in correctional settings is an important public health concern because of the risk that incarcerated populations may transmit the disease when they return to the general population. TB levels in South African prisons are about seven times higher than that of the general population due to overcrowding and limited health care access. However, few studies have examined TB rates among prisoners in Africa.

Methods: We quantify and compare the prevalence of TB between the prison and general population using the South African National Health Laboratory Service (NHLS) database on all TB tests performed in public health facilities between January 2004 and December 2011, including over 5 million patients. We extracted unique patient identifiers, test date, province, type of health facility, and basic patient demographics. We examined patterns by province, age, and sex.

Results: TB testing levels increased and TB prevalence rates decreased among the general and incarcerated population over time and follow similar patterns (Figure A). The incarcerated population demonstrated higher multi-drug resistant TB (MDR-TB) rates than the general population (Figure B). These results held for the general and the male population, particularly among those aged 21–30 years, which make up a large proportion of the incarcerated population.

Conclusions: The similar patterns in TB prevalence rates among the incarcerated and general population suggest that prisons are an important link in TB transmission. Incarcerated populations may be a disease reservoir, increasing TB transmission into the general population. Prisons are therefore critical sites for efforts to reduce TB rates in the general population.



PD-949-28 Results of the first mass screening campaign for tuberculosis in the Namibian Correctional Service

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Background and challenges to implementation: Namibia is a Southern African country with an estimated incidence of TB (561/100 000). Correctional settings (prisons) present a congregate setting with high risk for TB transmission. By 2015 no routine screening was done in the Namibian correctional setting, with the burden of TB unknown.

Intervention or response: Officials from correctional facilities were trained after consultation and joint planning between the National TB and Leprosy Programme and the Namibia Correctional Service. Screening was done for staff (correctional officers), inmates (offenders) and recruits (trainee officers) for key symptoms of TB (presence of cough, night sweats, fever, weight loss, and swollen lymph nodes), HIV and other medical history. Any positive response on the symptoms led to sputum collection and testing using smear

microscopy and Xpert MTB/RIF. NCS health-care staff conducted the screening with assistance from local health care workers.

Results and lessons learnt: 11 correctional facilities and the sole training college participated. Of 3114 inmates, 1495 participated (48%), and 374 (25%) correctional officers out of 1505. At the training college, 225 trainees were screened out of 325 (69%). Those found to have symptoms were 406 inmates, 68 officers and 4 recruits. All those with symptoms had sputum collected and 3 inmates, 1 officer and 1 trainee were found to have bacteriologically confirmed TB. Also of note is that 13% of inmates, 10% of officers and 1% of trainees had been treated for TB before, while 48% of inmates, 83% of officers and 9% of trainees were aware of their HIV status

Conclusions and recommendations: Mass screening for TB in correctional settings is feasible even with limited resources. Trends should be monitored though bacteriologically confirmed TB was lower than other reports in correctional settings. Periodical mass screening of TB was introduced following this campaign in addition to plans for mandatory admission and exit screening. High stigma against TB and concern with job security (yet 10% previously treated for TB) prompts the need for targeted TB awareness campaigns. The low knowledge of HIV status among recruits suggests need for promoting/access to counselling and testing services at the college.

PD-950-28 Is symptom screening sufficiently sensitive for identification of presumed tuberculosis patients in a congregate setting?

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Background: Luzira prison, located in Kampala City, is the maximum prison setup in Uganda. Within this prison is a training school where an estimated 2000 prison warders are trained every year. It is a requirement of this institution that all entrants that are meant to stay for a long period including prisoners and trainees are screened for TB to ensure early identification of TB cases, initiation of treatment and reduced risk of TB transmission. We therefore conducted TB symptom screening for prison warder trainees at Luzira in the first one month of the training.

Intervention: All the trainees were screened for TB using the designed screening tool. Symptoms included were, cough for two or more weeks, history of having coughed blood, loss of weight in the last three months, recent loss of appetite, chest pain and night sweats in the last three weeks.

Results: A total of 1744 trainees were screened of whom 68% were males, their mean age was 24 years. Of these,

183 (10.4%) trainees reported at least one symptom. Seventy six (4.4%) reported cough for more than two weeks, of which 9 (0.5%) had coughed out blood, 20 (1.1%) had loss of appetite, 67 (3.8%) loss of weight, 59 (3.4%) reported chest pain and 27 (1.5%) had history of night sweats in the last three weeks. Of the total patients with cough, 20 provided sputum samples for analysis all of which tested negative on microscopy. Due to high likelihood of TB in one of the trainees based on signs and symptoms, the clinician ordered a chest X-ray which was sufficiently suggestive to start the patient on anti-TB treatment.

Conclusion: Considering findings of the recently concluded national TB prevalence survey in Uganda at 402 cases per 100 000 population, about seven cases from this population were expected although only one case was identified moreover by radiological means. We conclude that symptom screening alone may not be sufficiently sensitive to identify presumed TB patients in this population. Other screening approaches should be explored to minimize missed opportunities for identification of presumptive TB patients.

PD-951-28 Successful involvement of ASDAP in the management of tuberculosis cases in the central prison of Bamako, Mali

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Background: Tuberculosis in prisons is a serious challenge for National Programs fighting against this disease mostly in developing countries. In 2013, a study involving 1900 prisoners from three prisons in Mali showed 28 cases. The notified cases were 36 times higher in prisons than in the general population. Among these cases 67% ended their treatment, 29% were lost, 7% were co-infected and 7% were dead during the study. These results showed that the management of TB in prisons of Mali needs to be strengthened.

Intervention: In 2014, the Non-Governmental Organization ASDAP (Population Aid and Development Association) assigned a medical officer to the prison in Bamako. He provided medical assistance to the 1.800 prisoners on average against some diseases such as malaria, tuberculosis and HIV/AIDS. The medical officer offered HIV test to all prisoners at the entrance after counseling process. Once, presumed cases of tuberculosis were identified, sputum were collected and sent to the Health Center for microscopy. He notified each diagnosed tuberculosis case to the nurse in charge of treatment and verified if TB patients were co-infected TB-HIV or not. Co-infection cases received ARV to better ease the tuberculosis disease management.

Results: The presumed TB patients among prisoners were 93 in 2014-2015, tuberculosis cases were 45, among them 18 cases in 2014 and 27 cases in 2015 compared to

23 in 2013. Among tuberculosis patients, 4 cases (22%) of co-infection TB-HIV were detected in 2014 compared to 2 cases (7%) in 2013. The proportion of patients who completed treatment was 73% in 2015, 100% in 2014 and 67% in 2013. In 2015, the proportion of patients who was lost during processing was 26% compared to 29% in 2013. These results showed that this intervention has allowed an improvement in the quality of medical care with zero death due to tuberculosis and it contributed to decrease the rate of lost in prison of Bamako.

Conclusion: The intervention of ASDAP provided a successful model for management of tuberculosis in prisons. This initiative deserves to be extended to all prisons in Mali.

PD-952-28 High incidence of tuberculosis infection and disease in twelve Brazilian prisons

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Background: Prisons are optimal environments for TB transmission and globally, have the highest TB incidence rates.

Methods: We performed a prospective cohort study of prisoners from 12 prisons in the 5 largest cities in the state of Mato Grosso do Sul, Brazil, in order to assess TB infection and disease rates, and evaluated the impact of annual screening in Brazilian prisons. From 7221 inmates in the 12 prisons, we recruited 3771 for the study, and 3380 (90%) consented to participate and were enrolled. After 1 year, 1,422 participants remained incarcerated in the same prison; this subset comprises the prospective cohort in whom TST conversions and TB incidence were assessed. We administered a baseline questionnaire and tuberculin skin test, followed subjects for 1 year in cohort study, and performed a repeat TST. TST positivity was defined as ≥ 10 mm (≥ 5 mm for HIV-infected individuals). TST conversion was defined as ≥ 10 mm induration and at least 6 mm increase in size of induration in a subject during follow-up who had a baseline TST ≥ 10 mm. We used Cox Proportional Hazards Models to estimate crude (CHR) and adjusted hazards ratios (AHR) for active TB.

Results: We found an annual risk of tuberculosis (TB) infection of 26% (95%CI 23-29) and incidence of active TB of 1771 (95%CI 1115-2614) cases per 100 000 population. Cases identified through active screening were less likely to be smear-positive than passively detected cases (10% vs. 51%; $P < 0.01$), suggesting early case detection. However, there was no reduction in

incident disease among individuals actively screened vs. those not screened (1.77% vs. 1.69%; $P = 0.95$). TST conversion and incidence of active TB were higher in male compared to female prisoners (28% vs. 10%; $P < 0.01$; and 1.94% vs. 0.53%, respectively; $P = 0.18$). Reported productive cough at baseline (AHR 2.63; 95%CI 1.13-6.15) and drug use over one year (AHR 3.93; 95%CI 1.31-11.79) were associated with active TB during one year of follow up.

Conclusions: The high rate of incarceration and movement combined with extraordinary infection rates, indicate that prisons can be important reservoirs of TB transmission to the general population.

PD-953-28 Tuberculosis case finding in a Brazilian prison

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Background and challenges to implementation: In Brazil, almost 70 000 new cases of tuberculosis (TB) are notified per year, and 7.6% of the cases are found in inmates. In 2013, the National Tuberculosis Program (NTP) submitted a project for the TB Reach in order to increase the case detection in prisons, through systematic screening for cough and X-ray, and implementation of Xpert MTB/RIF. This summary describes the results obtained at the Porto Alegre Central Prison (PACP).

Intervention and response: In Porto Alegre, there are eight prisons, with about 6000 prisoners. The PACP lodges 4400 inmates. The prison is a temporary institution that receives the inmates and then transfers them to other prisons in the state. From October 2014 to December 2015, we screened prisoners for TB considering the presence of cough and abnormal X-ray results. For the positively screened, sputum sample was collected for laboratory investigation. We monitored the project data and NTP information system quarterly.

Results and lessons learnt: We investigated 8787 inmates in the PACP. Of these, 2697 (30.7%) had cough or an abnormal X-ray. 1493 (55.4%) prisoners were investigated with Xpert and 213 (14.3%) confirmed. In addition, another 25 cases were confirmed by smear microscopy or culture. The prevalence rate found was 5409 per 100 000 prisoners. NTP-Brazil data showed an increase in the number of cases reported on prisoners in Porto Alegre, after the start of the project, with linear trend ($y = 55.1 + 16647x$; $R^2 = 0.4063$). An increase was also observed in the control population, however, less than what we observed in the evaluated population ($y = 84.65 + 0,7324x$; $R^2 = 0.0721$).

Conclusion and key recommendations: The positivity of patients with TB and the prevalence rate showed high risk for TB in the PACP. The results of this intervention were demonstrated in the notifications of TB cases reported to NTP. Still, the goal set at the beginning of the project, to detect 900 cases, was not reached. There are some reasons for this result: 1) operational problems that

occurred during the project; 2) short time to evaluate the intervention, and 3) targets were overestimated.

PD-954-28 Getting diagnosed: the use of A&E and factors associated with delays among pulmonary TB patients in London, 2013–2014

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Background: Early diagnosis remains the most effective tool against TB transmission. London TB patients often report visiting accident and emergency (A&E) departments prior to diagnosis, a service designed and intended for urgent care. We aimed to describe which patients first presented to A&E, and what factors were associated with delays to diagnosis, both before and after presenting to the healthcare system.

Methods: We analysed surveillance data from London TB Cohort Reviews on pulmonary TB cases notified between January 2013 and June 2015. Logistic regression was used to determine risk factors for: first presenting to A&E, patient (from symptom onset to presentation) and healthcare system (from presentation to treatment start) delays.

Results: Of the 1777 TB patients included in the study, 33% (496) first presented at A&E. There was strong evidence of an association between A&E presentation and homelessness (aOR 2.4; $P < 0.0001$). Patient delays of ≥ 30 days were experienced by 62% (638) of individuals. Patient delays were associated with imprisonment (aOR 2.1; $P = 0.040$), and increasing age (linear aOR 1.3; $P = 0.005$). Healthcare delays of ≥ 30 days were reported by 40% of patients (577), and associated with sex (males less often delayed, aOR 0.71; $P = 0.005$) and where they first presented (patients presenting at A&E were less likely to be delayed, aOR 0.21; $P < 0.0001$).

Conclusions: A&E presentation was a common feature among London TB patients. It was particularly common among homeless patients, which may be due to poor engagement with alternative primary care services. After attending A&E, however, patients were diagnosed more quickly than those presenting by other means. Additionally, after controlling for A&E presentation, females were more likely to experience delays within the healthcare system itself. Patient delays were more common among older patients and those with a history of imprisonment. Further exploration of the reasons behind these findings will help us understand and reduce delays among vulnerable patients, thereby improving patient experience and reducing the risk of onward transmission.

35. From TB data collection to TB data use for decision making

PD-955-28 Improving TB patient indicators through frequent and prompt data use: a shift from quarterly to monthly data collection in Kampala

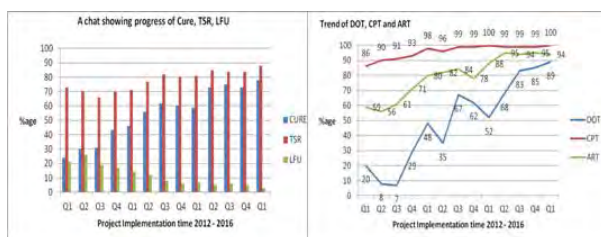
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Background: Kampala City is the highest TB burdened district in Uganda with about 7500-8500 cases notified to annually. By January 2013, the city had a loss to follow up (LFU) rate of 21%, directly observed therapy (DOT) coverage of 27%, cure rate of 30%, and treatment success rate (TSR) 73%. The CPT and ART coverage among the HIV co-infected were at 86% and 59% respectively. Prior to 2012, TB data had been collected every 3 months to match the reporting requirements of the national program. We present improvement in TB control indicators above partly contributed to by the reduced reporting intervals from 3 times a month to monthly as well as use of a monthly dashboard of indicators.

Intervention: Since January 2013 with support from its partners, Kampala Capital City Authority (KCCA) implemented monthly TB data collection and use of this data to monitor key TB control indicators for quarterly reporting. The aim was to identify gaps patient management as well as status of indicators. A list of patients and indicators that needed to be followed up was generated for individual health facilities for TB supervisors to make follow up with health facility management and community health workers as well as a circulation of a monthly dashboard of indicators.

Results: By January 2016 the cure rate has improved to 78%, TSR to 88%, DOT coverage to 89%, 100% and ART coverage to 94% (Figure).

Conclusions: Monthly data use contributed to the improvement of key performance indicators for TB patients in Kampala. This is probably a useful intervention that needs to be expanded to other facilities and urban settings with similar challenges to facilitate routine and timely data use as one of the ways to improve performance.



PD-956-28 Assessment of TB performance indicators: a comparison of public and private health sectors in Kenya

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Background: Involving Private Providers (PPs) in TB control has been embraced as an approach to improve people's access to good TB care in settings where private providers offer better geographical coverage and areas where there is preference for the sector. However, the clinical management practices of private are often inadequate; they have been shown to prescribe inappropriate treatment for diseases (Lönnroth K, 2003). Despite the continuous implementation of Public-Private Partnership (PPM) in TB control in Kenya, a comparison of performance indicators between public and private sectors has not been documented. The overall objective of this study was to compare the performance of private and public health sectors in Kenya in terms of TB control indicators.

Methods: Secondary data from the National TB program database was used. Data for 2013 and 2014 from TB electronic surveillance system (TIBU) was cleaned and analyzed and a comparison computed between the private and public sectors.

Results: In 2013 and 2014, 10% of notified cases in private sector were children, while in public sector the proportion dropped from 10% to 9%. HIV testing of TB cases for both 2013 and 2014 public sector attained 95% while private sector attained 93%. ART uptake among the TB-HIV co-infected in public was 87% and 86% and in private was 85% and 87% in 2013 and 2014, respectively. Nutritional assessment in private sector was 24% and 19% in 2013 and 2014, respectively, while in public sector it was 15% for both 2013 and 2014. The Treatment Success Rate for smear-positive TB cases was 89.4% compared to 88.1% in public sector.

Conclusions: The findings of the study showed that private sector and public sector have similar performance indicators, and the former poorer performance may have been influenced by poor sensitization of the private sectors. However, in most indicators the performance is lower than the targeted rate for both sectors. The analysis suggests that there is need for an effective intervention package that includes the private providers, public health workers and the staff of the national TB program to ensure achievement of all the targets by both sectors.

PD-957-28 Estimating under-reporting of tuberculosis cases in the national surveillance system in Japan: comparing surveillance data and vital statistics

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Background: Surveillance of tuberculosis (TB) disease is essential for TB prevention and control. Evaluating the performance of TB surveillance is important even in the countries where effective TB surveillance already exists. Although inventory studies, e.g. capture-recapture studies, are recommended to investigate under-reporting of TB cases, the nationwide studies have not been conducted because of the limitation of access to the individual record in other databases in Japan. The objective of this study is to estimate under-reporting of TB cases in surveillance in Japan by using the simple method.

Methods: TB death was estimated according to the following equation: $D = N\beta_1 + M\beta_2$

Where D denotes number of TB deaths, N denotes number of notified cases in surveillance, M denotes number of not notified cases, β_1 and β_2 denote case fatality rates notified and not notified, respectively. Case fatality rates of notified patients after one year from the notification until after eight years were calculated by death information in TB surveillance. We assumed that most of the not notified cases were not treated, case fatality rate of not notified was assumed to 0.43 (range 0.28-0.53). Using the number of TB deaths in vital statistics, the number of not notified cases was calculated in 2012, 2013 and 2014. The under-reporting rate was estimated by average of these 3 years.

Results: Estimated case fatality rates of notified patients as shown in Table 1. Case fatality rate after 8 years was 6%, and 80% of TB death occurred in the first year. The number of TB death in vital statistics, estimated TB death notified and not notified and estimated under-reporting as shown in Table 2. Under-reporting rate was estimated to 6.3% (5.1%–9.3%).

Conclusions: There were substantial differences of TB death between TB surveillance and vital statistics. These differences suggested the under-reporting of TB notification after death in TB surveillance.

Table A) Estimated case fatality rates of notified patients, **B)** Estimated number of TB deaths in vital statistics

A)

Years after notification	<1 year	1-2 years	2-3 years	>=4 years
Case fatality rate(%)	4.6	1.1	0.1	0.1

B)

TB death (vital statistics)	Estimated TB death notified	Estimated TB death not notified	Estimated number of underreporting
2097	1446	651	1516 (1230-2328)

PD-958-28 Underreporting of tuberculosis cases in the Notifiable Disease Information System in Brazil

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Background: Underreporting of diseases that are relevant to public health is a major challenge for health surveillance since it makes it impossible to understand the real magnitude of these diseases. The aim of this study was to analyze the underreporting of tuberculosis cases in the Reportable Disease Information System (Sinan) in Brazil as from the Mortality Information System (SIM).

Methods: A descriptive cross-sectional study was carried out of the TB cases underreported at Sinan in the years 2013 and 2014. To estimate the underreporting was performed a probabilistic record linkage between deaths reported to SIM in 2014 and tuberculosis cases reported to Sinan in 2013 and 2014, using RecLink III software. Deaths considered underreported in SIM were deaths with basic or associated cause of tuberculosis (ICD-10 A15-A19) that were not linked to any notification of Sinan, or was linked but the date between the tuberculosis diagnosis and death was higher than 270 days.

Results: In 2014, 7105 tuberculosis deaths were reported (4376 basic cause, and 2729 associated cause). Of these, 2893 deaths were not reported to Sinan, resulting in a 40.7% of underreporting. Among underreported deaths, 72.5% were male, 56.6% were in the 35-64 years old age group, 62.9% were black and 71.6% only completed elementary school. The basic cause HIV/AIDS accounted for 57.3% of the deaths in which tuberculosis was mentioned as associated cause and which was not reported in Sinan, followed by chronic obstructive pulmonary disease (COPD) (3.5%) and acute myocardial infarction (AMI) (1.9%).

Conclusions: There was a high proportion of underreporting of tuberculosis cases that progressed to death and were reported in the SIM, not in Sinan. This may show a failure in providing services to patients with tuberculosis, especially with regard to early diagnosis of quality and proper treatment, once these cases are already entering in the services featuring advanced stages of disease and progressing to the worst outcome.

PD-959-28 Availability of bacteriological information in tuberculosis notification data in Germany

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Background: Laboratory confirmation including culture and nucleic acid amplification test (NAAT), and drug susceptibility testing (DST) are essential for an appropriate tuberculosis (TB) diagnosis and therapy. Moreover, molecular surveillance based on *Mycobacterium*

tuberculosis genotyping relies on microbial cultures to obtain mycobacterial DNA. We aim to determine how often bacteriological culture, NAAT and DST are reportedly done among notified pulmonary TB cases in Germany to assess coverage of drug resistance information and eligibility of cases for molecular surveillance.

Methods: We used German case-based 2002-2014 TB notification data (clinical case definition). We calculated how often (in %) among pulmonary TB patients (overall and in children) information on mycobacterial culture, on either culture or NAAT, and on at least isoniazid and rifampicin DST were available and lead to a positive result.

Results: From 2002 to 2014, 52 960 pulmonary TB cases were notified. Of those, 520 were in children aged 5-9, and 989 in children aged < 5 years. Mycobacterial culture was reportedly performed in 94% of all pulmonary TB cases (5-9 year-olds: 83%; < 5 year-olds: 89%). Among them 77% were positive (5-9 year-olds: 38%; < 5 year-olds: 55%). In 96% of all cases either culture or NAAT were reportedly done (5-9 year-olds: 87%; < 5 year-olds: 92%) with 80% positive results (5-9 year-olds: 44%; < 5 year-olds: 61%). Among culture- or NAAT-confirmed cases, 89% had information on both isoniazid and rifampicin DST (5-9 year-olds: 77%; < 5 year-olds: 85%); and 2.5% had a multidrug-resistant (MDR) strain (5-9 year-olds: 4.4%, < 5 year-olds: 2.3%). Of all notified pulmonary TB cases, 70% had DST information to evaluate MDR (5-9 year-olds: 30%; < 5 year-olds: 48%).

Conclusions: Overall bacteriological investigation of pulmonary TB is largely done and documented in German notification data. A high proportion of TB cases are bacteriologically-confirmed and therefore eligible for drug resistance and molecular surveillance. However, in children aged 5-9 years the coverage of laboratory testing was reportedly lowest, and bacteriological confirmation less often achieved. Here, additional efforts in specimen collection, bacteriological investigation and reporting might be beneficial in view of adequate treatment and to exploit the full potential of molecular surveillance.

PD-960-28 Research and programmatic agendas since 2000 in Cambodia: HIV, tuberculosis and malaria

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Background: Coordination and strategic planning of health sector rehabilitation and research is often weak during periods of political transition and unprecedented aid inflows, a situation Cambodia has experienced over recent decades. Although HIV, tuberculosis (TB) and malaria have been a major focus of funding and disease

control efforts, research output on these diseases has not been investigated previously. The aim of this systematic scoping review is to analyse trends in publications on these three communicable diseases in order to identify evidence gaps and suggest future research needs.

Methods: We searched three electronic databases - Pubmed, Embase and Index Medicus for the South East Asia region (IMSEAR) - and additional grey literature sources for studies on HIV, TB and malaria published between January 2010 and October 2015. Information about the disease area of focus and the methodology was extracted from all studies meeting the inclusion criteria.

Results: We reviewed 2581 unique studies of which 712 were included in the analysis. Our results demonstrated that while there has been a steady increase in the number of publications, there were much fewer publications on TB (16%), than HIV (43%) and malaria (41%). Observational epidemiological studies greatly outnumbered all other methodologies (44%), with limited research in other disciplines.

Conclusions: Despite substantial investments, some important research areas appear to have been neglected in Cambodia; specifically, studies on TB, and studies involving economic, qualitative, interventional and genomics methods are under-represented. The disparity in HIV, TB and malaria research in Cambodia identified by this review, considered alongside the disease burden suggests that an increase in TB research may be needed to inform control strategies. As countries such as Cambodia transition to a more stable period with reductions in funding, increased coordination in research priority setting may be important for generating evidence to inform disease control policies and resource allocation.

PD-961-28 Universal Access to TB Care (UATBC): information technology platform to drive scale-up in private sector engagement

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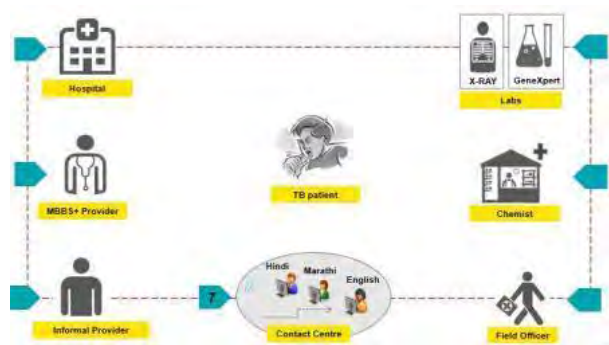
Background and challenges to implementation: In Mumbai, a Private Provider Interface Agency (PPIA) engages private providers to facilitate quality TB diagnostic and treatment services. Due to the sizeable scale of operations, a cloud-based application was deemed necessary to serve as force-multiplier for staff and facilitate effective patient management.

Intervention or response: To facilitate efficient patient registration and tracking, the Universal Access to TB Care (UATBC) application supports patient registration, and tracking of the beneficiaries from TB diagnosis till treatment, and treatment adherence monitoring. System generated e-vouchers are utilized to provide free diagnostics and anti-TB drugs to beneficiaries, with electronic transfer of voucher reimbursements to laboratories and chemists, making payment reconciliation simple and timely. UATBC is integrated with Nikshay, the national

TB programme's cloud-based application for notification of TB patients. UATBC system also triggers SMS alerts and reminders to providers, field officers and patients on various pre-defined events to support patient management. UATBC captures every patient's treatment information and end-to-end, reports and dashboards get generated from the system for case management. A dedicated contact center provides support in data entry, treatment adherence, and follow up activities of the patients.

Results and lessons learnt: With UATBC application and contact center support, just 17 field staff have engaged and supported 2700 providers (doctors, chemists, laboratories). Till date, more than 15 000 TB patients have been registered and notified to the national TB program and are being tracked through UATBC. For these patients, more than 21 000 drug vouchers and 6000 diagnostic vouchers have been issued. And, for these vouchers, more than USD 600 000 has been electronically disbursed to various diagnostic centers and chemists in a timely manner, and 12 000 patients are being supported for treatment adherence.

Conclusions and key recommendations: Cloud-based applications such as UATBC serve as a force multiplier and can play a critical role in effectively and efficiently engaging private providers thereby helping transform TB control in Mumbai.



PD-962-28 Improving the quality and usage of MDR-TB surveillance data in South Africa

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Background: The multidrug-resistant (MDR) tuberculosis (TB) crisis is accelerating, yet an estimated 70% of MDR TB cases are missed by national TB systems. As MDR TB treatment is decentralized, it is crucial that facilities are equipped to accurately record and report all cases to improve national reporting and inform facility management.

Intervention: The South Africa National Department of Health (NDoH) partnered with the U.S. Centers for

Disease Control and Prevention (CDC) to design and pilot a novel facility-based approach to engage staff at MDR TB treatment sites to accurately record, report, and analyze MDR-TB surveillance data [TB Data: Informing Quality and Usage (TB-IQu)]. This approach involved three steps to foster organizational change: 1) a situation assessment to identify challenges and opportunities for MDR-TB data recording, reporting, and analysis; 2) a workshop to develop and implement plans to improve data recording, reporting, analysis, and dissemination; and 3) teaching facilities to analyze, interpret, and utilize their data. Assessment tools, teaching curriculum, facilitator guides, and an analysis template were packaged for easy implementation.

Results and lessons learnt: TB-IQu South Africa was implemented at three MDR-TB treatment facilities in KwaZulu Natal Province. Data capturers, hospital administrators, MDR-TB nurses, and monitoring and evaluation staff examined and streamlined processes for MDR-TB data recording, reporting, review, and analysis and developed skills to analyze MDR-TB data. Time series analysis identified gaps that could be reconciled to improve case notification and MDR-TB management. Facilities discovered untapped potential in engaging the hospital's monitoring and evaluation staff to support routine review and analysis of MDR TB data. On-going support by district and provincial staff is necessary to ensure implementation of standard operating procedures for data, including routine data analysis.

Conclusions: TB-IQu South Africa is strengthening MDR-TB surveillance at facilities by streamlining recording and reporting processes and actively reviewing MDR-TB data. The NDOH should continue to roll out TB-IQu in MDR-TB sites and monitor its acceptance and viability over time. This approach can be easily adapted in other countries to improve accuracy of case notification by engaging facilities with TB surveillance.

PD-963-28 Promoting evidence-informed policy making: lessons learned from setting up the NDOH TB Think Tank in South Africa

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Background and challenges to implementation: TB is a major health problem in South Africa (RSA). In response to this, the country has become an early adopter of innovation to change the face of the epidemic. A wealth of expertise and data exists in RSA that can be optimized to inform TB decision making, but often is underutilized.

Intervention or response: Could a dedicated TB Think Tank, embedded in the RSA National Department of Health (NDOH), and tasked with anticipating and responding to policy maker requests for quantitative analysis, better support TB control policy and implementation decision-making? Support was provided from

the BMGF for activities including: quarterly f2f Think Tank meetings, dedicated epidemiological and economic staff, convening of regular calls with a wider network of unpaid expert advisers in an Executive Committee and three area specific Working Groups: covering data for policy, implementation and research.

Results and lessons learnt: The RSA TB Think Tank was set up in 2014 and the Secretariat based at the research institute Aurum. Despite initial enthusiasm, motivating participation from NDOH and external experts proved challenging and had mixed results, perhaps in part due to incomplete understanding of policy environment/capacity constraints. Motivation of working groups was most successful when aligned with a visible NDOH decision, and/or focussed on a specific question. Despite these challenges, the Think Tank, with partners, contributed to a successful and first ever joint investment case for TB-HIV. Evidence created by the Think Tank, and partners, contributed to the decision by the RSA government to create the first ever conditional (ringfenced) grant for TB in South Africa, funded with ~500m ZAR of new funds for TB. These funds are being used, in part, to guarantee national access to/sustainability of GeneXpert rollout.

Conclusions and key recommendations: The RSA NDOH government Think Tank, and partners, has yielded some success in supporting evidence-informed decision making, and increased funding for TB in RSA. Redesigning the technical assistance components and identifying ways to increase involvement of NDOH staff and the wider network of experts may facilitate higher impact. Government led Think Tanks may be replicable in other countries.

PD-964-28 The impact of tuberculosis risk scores for child contacts on timely uptake of treatment for latent infection

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Background: Tuberculosis Risk Scores for Child Contacts, an eight point scoring system for child contacts aged younger than 13 years, published in early 2014 in AJRCCM includes 4 items: the contact's tuberculin skin test (TST) induration, index patient's smear results, area where index patient lives and index patient's gender. Automatic calculations in TB case management system and an app of mobile phones for the score have been available since 2015 helping care providers to prioritize children LTBI treatment.

Intervention: To evaluate whether the implementation of this e-health module for the score improved the timely uptake rates of treatment among high-risk child contacts (scores ≥ 4). Data was collected in 2010 and 2015 from TB contacts aged ≤ 13 years who had received TST during contact investigations with an before and after

cohort design. Contacts with scores ≥ 4 were analyzed using 2 indicators: the interval between TST administration and commencement of LTBI treatment and uptake rates of LTBI treatment < 30 days after TST administration. The data was obtained from the National Surveillance Network of Communicable Disease, Centers for Disease Control, Taiwan on 1 March 2016.

Table Univariate and multivariate analysis of timely uptake of treatment

Characteristics of contacts	Uptake rates	univariate		multivariate		subgroup multivariate	
		<21 days	Relative risk (95% CI)	<21 days	Relative risk (95% CI)	<21 days	Relative risk (95% CI)
	n=1448					For 5-12 year-old group N=1411	For female group N=1119
Age of contacts	0-4	454 (74%)	1.20 (0.97-1.49)	1.198 (0.97-1.49)			268 (72%)
	5-12	989 (70%)					503 (67%)
Gender of contacts	Male	672 (74%)	1.29 (1.06-1.57)	1.303 (1.07-1.59)	486 (73%)	1.32 (1.05-1.66)	
	Female	771 (69%)			503 (67%)		
Year of LTBI treatment	2015	742 (73%)	1.22 (1.01-1.48)	1.196 (0.98-1.45)	467 (72%)	1.34 (1.06-1.68)	402 (72%)
	2016	701 (69%)			513 (67%)		369 (65%)
Score	4	872 (72%)	1.07 (0.88-1.30)	1.065 (0.88-1.30)	589 (71%)	1.08 (0.86-1.37)	450 (68%)
	5-8	571 (70%)			400 (69%)		321 (70%)

36. TB testing: a bouquet of approaches

PD-965-28 Evolving diagnostic algorithms to improve detection and cost-efficiency: a TB REACH project in Cambodia

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Background and challenges to implementation: Despite a significant reduction in TB prevalence following a decade of health system strengthening and economic growth, Cambodia still ranks as one of the 22 high TB burden countries. In an effort to expand care, Sihanouk Hospital Center of HOPE implemented an active case finding project among key populations. During its implementation, diagnostic algorithms evolved to simplify the flow of work, increase the number of people detected with TB and to reduce the cost per diagnosed patient.

Intervention or response: The project deployed a mobile chest X-ray (CXR), Xpert MTB/RIF testing, and LED-FM microscopy. For two quarters, the diagnostic algorithm was tailored to three key populations which involved symptom screening, then direct Xpert testing, Xpert testing after smear, or Xpert testing after smear and CXR. In the next quarter, we used a CXR screen on all key populations, then Xpert after CXR, or Xpert after CXR and first smear negative. In the following two quarters, we continued the same approach, but a single algorithm was applied to all key population, Xpert testing after CXR and first smear negative.

Results and lessons learnt: During the intervention we screened 314 360 people. Overall yield of bacteriologically-confirmed TB (SS+/B+) were consistent over the different algorithms, 0.95% (100 SS+/B+), 0.96% (45

SS+/B+), and 0.93% (130 SS+/B+) respectively. The yields of all forms were 6.1% (647 diagnosed), 6.8% (316 diagnosed) and 4.7% (652 diagnosed) in the corresponding periods. The costs per SS+/B+ patient detected were US\$ 181, US\$ 334, and US\$ 198, and all forms TB were US\$ 50, US\$ 78, and US\$ 63 in the respective periods.

Conclusions and key recommendations: The first period's algorithms were the most complicated to implement, but it was the most cost efficient. The second period's algorithms were less complicated, but it added more cost to find one SS+/B+ case, and the yield was not increased. The third period, the standard algorithms were used for all groups, the simplest to implement, the yield of case finding was the highest for SS+/B+ and all forms, and the cost were lower than the second period.

PD-966-28 Experience with computer-aided detection for tuberculosis through chest radiography of presumptive cases under a public-private mix initiative in Bangladesh

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Background: Chest radiography (CXR) can be used as an effective tool for systematic screening of presumptive pulmonary TB cases in high burden limited resource countries like Bangladesh. Human radiological interpretation varies with readers. Automated reading using computer-aided detection for TB (CAD4TB) has shown potential in different settings and need to be assessed at country level.

Methods: CAD4TB was evaluated under a public private mix initiative targeted to serve the presumptive pulmonary TB cases identified at practice places of networked Private Physicians (PPs) in Dhaka city. A network of more than 1800 PPs (specialists and general practitioners) referring presumptive cases were established. Presumptive TB cases referred by the PPs were enrolled for CXR from July 2014 to February 2016. CXRs were automatically scored using CAD4TB software into normal (CAD score < 40) and abnormal (CAD score ≥ 40) CXRs. The CXRs were also read by a certified radiologist for possible signs of TB who was blind to CAD score. All the presumptive TB cases irrespective of the CXR result were tested with GXP using single, good quality, spot sputum specimen and were compared with CAD4TB score and also with interpretation of the radiologist.

Results: CXRs and GXP tests were performed simultaneously among 18,269 presumptive TB cases. Among the cases, 15 118 (82.8%) had abnormal CXR score and 2727 were positive on GXP. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of abnormal CXR compared to GXP were 97%, 19.7%, 17.5% and 97.4%, respectively. The

sensitivity and NPV of radiologist's interpretation were 90.5% and 97.2%, respectively.

Conclusions: The higher sensitivity and NPV of CAD4TB compared to radiologist demonstrates the effectiveness of its use in the diagnostic algorithm as a screening tool in high burden settings. It can certainly be used in the gateway of advising expensive tests like GXP.

PD-967-28 RiView: an advanced computer-aided diagnosis platform for tuberculosis detection from digital chest X-rays

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Background: Chest X-rays are widely used in many settings, especially among private clinicians for diagnosis of lung symptomatic patients. However, variability in inter- & intra- reader agreement, wide ranges of sensitivity and specificity along with a lack of standard classification systems are well documented. The use of newer technologies like computer aided diagnosis (CAD) platforms for radiological image analysis and interpretation can further improve pulmonary tuberculosis interpretation from CXRs. RiView is an advanced lung abnormality detection CAD platform specifically trained on TB related radiological markers and is designed to offer differential diagnosis capability against other pathologies that mimic typical pulmonary tuberculosis abnormalities.

Methods: 1) Lung segmentation: Lung segmentation is performed using advanced regression analysis. During training, local binary features are extracted using a random forest and a regression model is trained. During testing, local binary features for each of the landmarks are predicted using the trained regression model. 2) Rib suppression: In order to suppress the ribs we take the rib vertical profiles of the gradient image and using the slope information rib locations for each profile is identified. Then local windowing operation is performed to match the local statistics of the rib region with the lung region. The rough edges are the post-processed using smoothing filters. 3) Abnormality detection – nodules: Probable candidate locations for nodules are identified from the rib suppressed images using various filtering techniques and morphological operations and finally the probable candidates are identified as ROI's. Descriptive features like geometric features and textural features are computed which are the fed to a random forest for the identification of actual candidates. A dual layered coarse to fine framework is applied which learns under the supervision of the descriptive features generated from the candidates. This framework with an accuracy of 96% behaves as a super discriminator by discarding challenging false positives while still achieving high sensitivity.

Results and conclusions: The novel lung segmentation and rib suppression technique presented are a prerogative for CAD algorithms for TB detection as they enhance abnormality detection algorithms.

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PD-968-28 Systematic screening with chest X-ray among hospital out-patients in Northwest Cameroon

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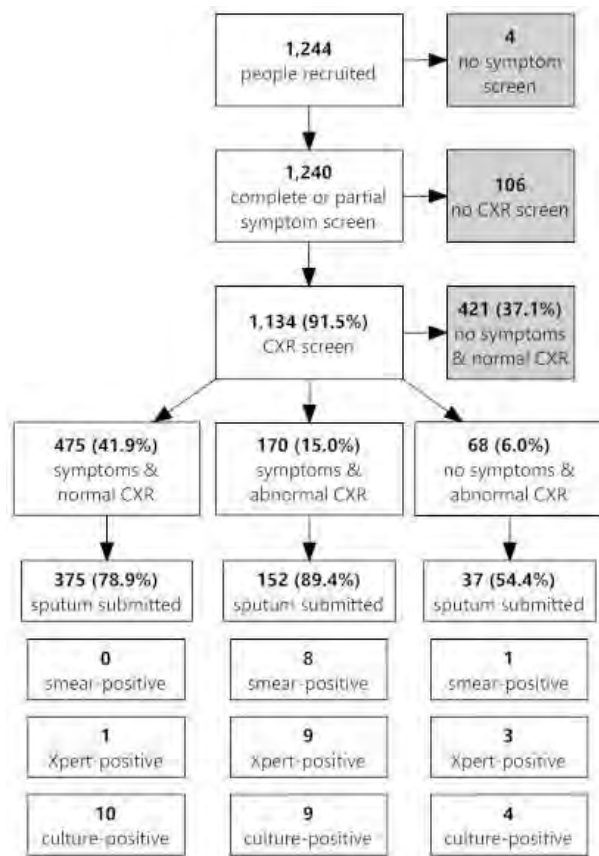
Background: Studies show many people with TB who visit health facilities fail to be diagnosed. In Cameroon, TB screening guidelines recommend a verbal questionnaire to identify people with one or more TB symptoms. As availability of stationary, digital X-ray systems increases, chest X-rays (CXR) may provide a complementary strategy to verbal screening for improving detection of TB among those already seeking care.

Methods: The first 25 people presenting at the Northwest Regional Hospital outpatient department each day were approached for inclusion in this study. Those consenting were verbally screened and received a free CXR. CXRs were graded as normal or abnormal with intentional over-reading in line with modern prevalence survey methods. Anyone with either one or more TB symptoms and/or an abnormal CXR was asked to submit sputum. Samples were then tested by LED-FM, the Xpert MTB/RIF assay and culture using both LJ and MGIT media. Preliminary laboratory results were abstracted from a patient database for analysis.

Results: To date 1244 people have been recruited, 1134 (91.5%) have been screened verbally and by CXR, 713 (62.9%) have been asked to submit sputum, and 23 (3.2%) of these have been diagnosed with culture-confirmed TB. Asymptomatic individuals with abnormal CXRs increased the total number of people with presumed TB by +10.5% and with confirmed TB by +21.1%. Individuals with TB symptoms, but a normal CXR comprise the largest group with presumed TB. Culture detected nine individuals with TB missed by Xpert in this cohort.

Conclusion: Adding CXR to verbal TB screening activities can improve detection of TB among people already seeking care. These results also highlight the limitations of LED-FM and Xpert, particularly among people likely to have paucibacillary TB.

Figure Study flow chart



PD-969-28 Strengthening TB diagnosis through informal doctors

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Background and challenges to implementation: Private provider Interface agency (PPIA) is engaged by Mumbai government for working with a network of private sector doctors to control TB. Malwani is a high density slum area of Mumbai with high TB suspects with multiple informal doctors being the first point of contact for TB suspects. PPIA offered Behavior Change Communication (BCC) for informal doctors to screen for TB aggressively among their suspected patients for early diagnosis.

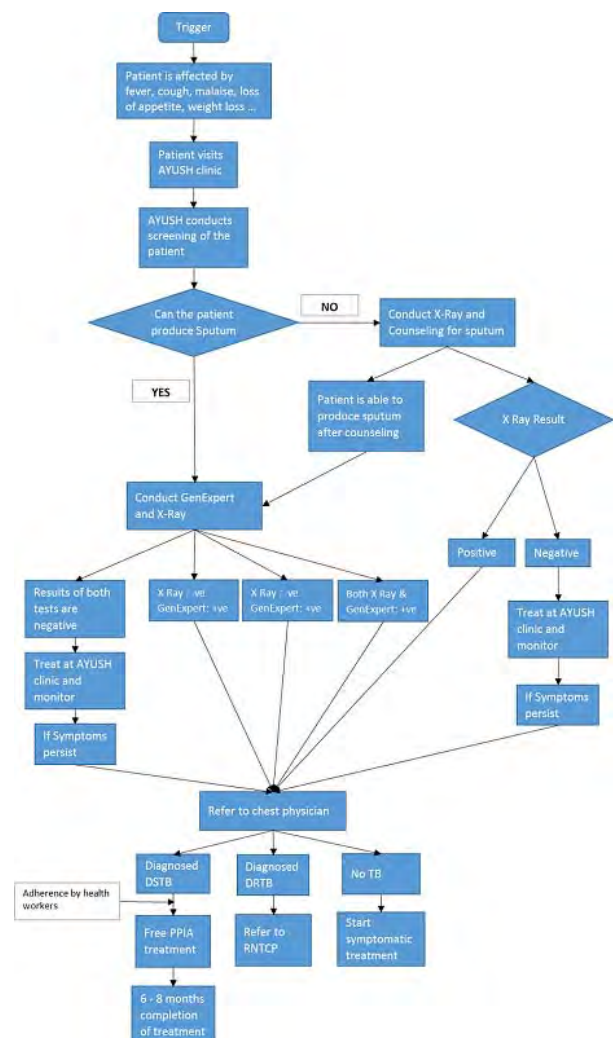
Intervention or response: With an objective for early diagnosis of TB, 25 informal providers, one laboratory, two chemists, one hospital and one chest physician (CP) were networked. BCC on upfront use of Chest X-ray and CBNAAT among the informal doctors was prorogated from November 2015 to December 2016 through three sessions by expert chest physicians. Free services included X-ray, CBC ESR, CBNAAT test, first line drugs for TB and adherence through health workers was offered to boost in the screening TB among informal doctors, with

all confirmed case being directed to qualified doctors through PPIA monitoring for further treatment.

Results and lessons learnt: In 3 months, registrations increased to 287 from negligible before BCC was conducted. 49 TB patients diagnosed, 46 started on free treatment, 38% sputum positive, 11% extra-pulmonary and 6% MDR cases. 268 free X-rays and 95 CB-NAAT sputum tests were conducted by the informal. From 32% of abnormal CXR, 55% underwent sputum testing (CBNAAT), 15% directly put on treatment. This shows many TB patients can be diagnosed at first point of contact, with the informal doctor's active participation in screening all TB suspects and directing them to qualified doctors for further treatment.

Conclusions and key recommendations: BCC with strong networking of informal doctors with the formal doctors for early diagnosis of TB was seen to be successful with more TB cases being diagnosed at primary level of healthcare. More networking of the informal doctors with help further detect the missing TB cases early in future.

Figure Early diagnosis of TB through informal doctors



PD-970-28 STAMP out TB: tuberculosis case-finding in the primary care setting

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Background: As of 2014, Indonesia had the second-largest burden of tuberculosis (TB) globally, with an incidence of 399 per 100 000 and a case detection gap of nearly 70%. Fortunately the country has a public health care system based on outpatient clinics, *Puskesmas*, that serve a population of >250 million. Based on these factors, we sought to evaluate an innovative approach to improving TB case-finding based in the public primary care setting in Jakarta.

Methods: The STAMP out TB initiative sought to improve TB diagnostic evaluation and increase TB case detection in primary care clinics by combining three synergistic interventions: 1) Training clinic staff in basic high-quality TB care; 2) Systematic screening of clinic attendees for TB based on presence of prolonged cough (≥ 2 weeks' duration); and 3) Regular monitoring, evaluation, and reporting of the quality of TB care back to clinic staff. The project was initiated September 2014 in 3 clinics in East Jakarta with a training for clinic staff in TB diagnosis and care, and the initiation of screening of all outpatient attendees. Performance feedback reports were introduced in February 2015.

Results: From September 2014 through August 2015, 65 746 patients were screened for prolonged cough. A total of 2793 patients (4.3%) screened positive, 565 (20.2%) were referred for TB evaluation, and 507 (89.7%) underwent TB evaluation, 51 (10.1%) of whom were found to have TB. The 51 cases constituted 19.9% of all TB cases reported from the clinics during this time period.

Conclusions: This pilot implementation of the STAMP initiative suggests that an approach to TB case detection incorporating cough screening, training, and performance feedback reporting in the primary care setting is feasible and effective at improving TB evaluation and increasing case detection in a high burden setting.

PD-971-28 Large-scale expansion of drug-resistant tuberculosis case-finding in Mumbai via private provider engagement

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Background and challenges to implementation: Mumbai is experiencing an unprecedented epidemic of drug-

resistant tuberculosis (DR-TB), but most patients are initially seen by private providers. Accordingly engagement of private providers in DR-TB case-finding is crucial to disease control. Indian standards of TB care require drug-susceptibility testing, but privately-managed patients experience cost and access barriers to DR-TB diagnosis and treatment. We deployed DR-TB diagnosis and referral services in Mumbai to improve DR-TB case-finding.

Intervention or response: Subsidized diagnostic testing, radiography and Xpert MTB/RIF (GX) was made available to private providers for use in presumptive TB cases via user-friendly e-voucher systems, managed by a private provider interface agency (PIIA). GX is provided free of cost to the patients at a private laboratory, or via the public sector. Sputum sample collection and transportation is conducted by field staff and the GX test report is available within 12-24 hours of sample collection. While rifampicin-sensitive patients usually remained with private providers, Rifampicin-resistant, were referred to a public health facility. PPIA managed the referral of patients from private to public sector.

Results and lessons learnt: From September 2014 to January 2016, private providers requested 11 537 GX tests, 3500 (30%) were TB positive, while 1,504 (13%) were Rifampicin resistant. Among these 526 (35%) were referred to the public sector for DR-TB treatment, and 752 (50%) were initiated private TB care with PPIA monitoring support. Mumbai's DR-TB case finding increased from 3665 in 2014 to 4906 in 2015, and in 2015 1274 (26%) were contributed by private providers via PPIA.

Conclusions and key recommendations: When provided access to free GX for patients and convenient interface services, Mumbai private providers contributed effectively to early DR-TB case finding and referral for supervised care. Expansion is underway.

PD-972-28 Further situation analysis of asymptomatic sputum smear-negative and culture-positive tuberculosis cases from the Cambodian prevalence survey in 2011

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Background: Previous study on sputum smear-negative, culture-positive (S-C+) tuberculosis (TB) from Cambodian prevalence survey 2011, presented in the 45th Union Conference, revealed that most TB cases had obvious abnormal shadows on chest X-ray (CXR). However, other information such as age, sex and symptoms were not included in the analysis. For giving information on process of screening TB cases in the community, further analysis was conducted, focusing on respiratory symptoms.

Methods: CXR films of S-C+ cases from the survey were categorized as follows; lesion side (right, left or both),

cavity (exist or not) and lesional expansion (class 1: less than 1/3 of unilateral lung field, class 2: 1/3 to whole unilateral lung field or class 3: more than whole unilateral lung field) and were measured. In addition, symptomatic case and asymptomatic cases were separated and compared.

Results: Excluding 3 cases without films and 3 cases without data, 206 cases were assessed. Of those, 87 cases (42.2%) had only right side, 37 cases (18.0%) had only left side, 80 cases (38.8%) had both sides and 2 cases had no shadow in terms of lesion side. Fifteen cases (7.3%) had cavitory lesion and 189 cases (91.7%) did not show any cavities. The numbers of cases which were classified to be 1, 2 and 3 were 127 (61.7%), 73 (35.4%) and 4 (1.9%), respectively. In comparison of 48 symptomatic cases and 158 asymptomatic cases, female were almost 40% in both groups. Average age (50.1 years vs. 58.1 years, $P = 0.005$) and lesional expansion class 3 (2 case vs. 0 cases, $P = 0.04$) had statistically significant difference.

Conclusions and recommendations: More than three quarters cases among S-C+ TB cases were asymptomatic and younger age group tend to be asymptomatic. For TB screening by symptom in the community, younger age group may miss out. To accelerate the current annual decline rate in TB incidence, we may need to diagnose more TB cases with S-C+ before converting smear positive. In addition, CXR screening is suitable especially for younger age group. To avoid over-diagnosis, sputum culture test and/or nucleic acid amplification test such as Xpert MTB/RIF and LAMP are required.

PD-973-28 Utilization of WHO-endorsed TB tests by private health care providers in Hyderabad, India

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Background: In India, private health care providers are a major source of tuberculosis (TB) care. There is paucity of information on how private health care providers utilise WHO endorsed TB diagnostic tests (GeneXpert MTB/RIF, solid, liquid culture & LED-fluorescence microscopy) for patient care. We report on the experiences of a major private medical laboratory (Helixer diagnostics) offering these tests in the city of Hyderabad, India (population ~5 million). The objective of the study is to describe the number and type of biological specimens that were requested for identification of TB through WHO endorsed TB diagnostic tests in this private laboratory.

Methods: We reviewed the laboratory records of Helixer diagnostics for the period March 2014 to February 2016 (2 years). We assessed the number of WHO endorsed tests that private providers ordered and their results.

Results: All tests were priced for patients as per the IPAQT coalition rates (USD 30 for GeneXpert, USD 2

for LED-FM, USD 14 for Liquid culture and USD 5 for solid culture; 1USD=INR 65). A total of 1180 specimens were requested for single/multiple tests from this laboratory. This included 612 sputum specimens and 568 biological specimens other than sputum (Pleural fluid, lymphnode tissue samples, cerebrospinal fluid tests, pus, bone marrow, peritoneal fluid). Gene-Xpert test and LED-FM were conducted on 870 specimens, liquid culture and DST was conducted on 361 specimens, and Solid Culture and DST on 27 specimens. Of the 1180 specimens that underwent testing, TB bacilli were detected in 318 samples. Rifampicin resistance was reported in 41 samples.

Conclusions: This is one of the first self-reports from a private laboratory from India, disclosing the information on the number of different types of WHO endorsed tests, types of specimens, TB bacilli and rifampicin resistance among patients seeking care in the private sector. Nearly half of the specimens were for diagnosis of extra-pulmonary TB, which is disproportionately higher, indicating that these tests were perhaps being used selectively. This could also reflect the characteristics of TB patients seeking care from the private health care providers, the knowledge and use of WHO endorsed tests by private health care providers.

PD-974-28 Relative effectiveness of free test vouchers on private provider TB test prescribing behavior in urban India

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Background: In India, private practitioners are often the first point of contact for patients with tuberculosis (TB) where misdiagnosis remains a concern, likely due to heavy reliance on bad quality TB tests. We distributed free vouchers of World Health Organization endorsed GeneXpert test among TB treating providers to understand if free vouchers of molecular TB tests can influence their diagnostic/prescription behavior.

Design and methods: In this pilot study implemented in Nashik (Maharashtra), 104 qualified private practitioners who interacted with TB patients and had not prescribed molecular tests for TB were randomly selected and assigned to either intervention or control group. Interviews were conducted to understand their baseline knowledge, attitudes, and practices (KAP) pertaining to TB diagnosis. Each physician in intervention group was given ten GeneXpert vouchers every month, for three months. Baseline interviews and observations were analyzed for indicators of diagnostic practices and knowledge of available TB tests. Both groups will be observed for their TB test prescription behavior for three months after the intervention period.

Results: Analysis of baseline KAP data showed that even though 54% of the sample had heard of GeneXpert test, more than 75% relied on non-specific tests such as chest

x-ray, smear microscopy, and Interferon Gamma Release Assay for pulmonary TB diagnosis. For extra-pulmonary TB cases, confidence on clinical judgement was placed above all tests. Physicians perceived GeneXpert as a test for confirming Rifampicin resistance, had limited knowledge about the test's sensitivity and specificity, quick turnaround time and ability to detect smear negative TB. This may have contributed to low utilization, with only ~10% free vouchers being utilized during the intervention period. More than 80% vouchers were utilized by one-sixth of all intervention group physicians.

Conclusions: Substantial dependence on non-specific TB tests and clinical judgement is widespread in the private sector, especially amongst general practitioners. Besides experiential learning, generating awareness on specific benefits of GeneXpert over other commonly used less sensitive tests, observing physicians' behavior after withdrawal of free vouchers, and understanding placement of GeneXpert in minds of physicians through an end-line survey might be useful in providing insights on factors affecting prescription behavior of private physicians.

37. TB mortality and recurrence

PD-975-28 Clinical parameters, routine inflammatory markers and *LTA4H* genotype as predictors for mortality among 552 tuberculous meningitis patients in Indonesia

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Background: Damaging inflammation contributes to the high mortality of tuberculous meningitis (TBM), but the link between cerebrospinal fluid (CSF) leukocytes and patient outcome is unclear. Recently, a Leukotriene A4 Hydrolase (*LTA4H*) genotype correlated with CSF leukocyte count and survival of TBM in Viet Nam. We examined clinical parameters, routine inflammatory markers and *LTA4H* genotype in a cohort study in Indonesia.

Methods: Adult patients presenting with suspected meningitis were included in a cohort, with prospective collection of clinical and laboratory parameters, including HIV-testing and CSF *Mycobacterium tuberculosis* microscopy, culture and PCR. Patients with suspected TBM received 6 months standard treatment and adjunctive dexamethasone. Patients were followed for more than one year, and survival analysis was done by Cox regression.

Results: Over a nine-year period, 998 patients were screened, of whom 552 were included with TBM. Two thirds (65%) were bacteriologically confirmed, and lowered consciousness (67%), cranial nerve palsy (58%), and motor dysfunction (52%) were common.

One-year mortality was 42.5% and strongly associated with HIV (HR 1.98). Among HIV-negative patients ($n=463$) with 96% follow-up, baseline Glasgow Coma Scale, fever, motor dysfunction, CSF protein, hypoglycorrhachia, *M. tuberculosis* culture, and high neutrophil counts in CSF and blood were significantly associated with higher mortality. The Leukotriene A4 Hydrolase (*LTA4H*) promoter polymorphism (rs17525495) was linked to CSF mononuclear cell count, but did not predict survival ($P=0.93$).

Conclusions: Late presentation and severity of disease probably account for the very high mortality of TBM in this setting. Fever, metabolic changes, and neutrophilic inflammation also seem to be linked to poor outcome. Further study is needed to characterise damaging immunopathology in TBM, and identify genetic markers to guide host-directed therapeutic strategies.

PD-976-28 A model-based estimation of lives saved by India's Revised National Tuberculosis Control Programme from 1997 to 2014

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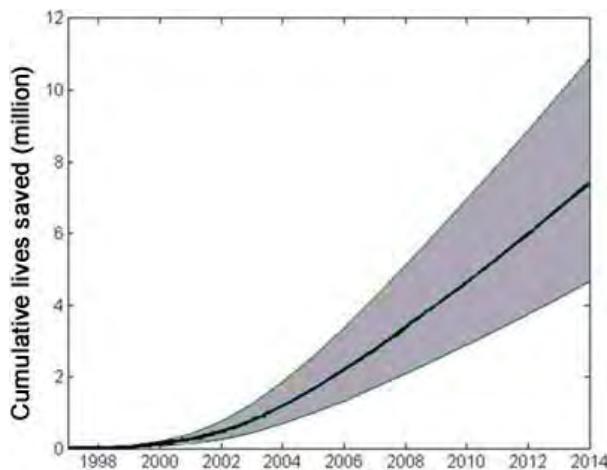
Background: The government of India launched the Revised National Tuberculosis Control Programme (RNTCP) in 1997, ultimately reaching nationwide coverage by 2006. To address the multidrug-resistant TB (MDR-TB) in a systematic way, the Programmatic Management of Drug-Resistance TB (PMDT) has been introduced under RNTCP since 2007. Patients on treatment in RNTCP suffered a lower mortality rate than those treated elsewhere (TBC India), due to lower rates of treatment failure and default, and higher rates of treatment initiation. Additionally, RNTCP services may have helped to reduce transmission of TB. We estimated how many lives were saved by RNTCP during these years, through both of these mechanisms.

Methods: We constructed a simple deterministic, compartmental model capturing the relevant mortality compartments, as well as TB transmission. Differential coverage rates of RNTCP has been adjusted over the years. We also conducted a literature search to build an evidence base for mortality rates at different stages of TB care. For the proportion of the population who are uninfected, having latent infection and who are cured, we assigned a natural mortality rate, reflecting average life expectancy in India. We used Bayesian methods to estimate uncertainty in the lives saved.

Results: India's RNTCP had an impact in averting TB transmission as well as in improving treatment outcomes. Overall we estimate that a total of 7.4 million TB deaths (95% C.I. 4.7–10.8 million) were averted due to the RNTCP, from 1997 to 2014 (Figure). About 27% amongst total lives saved are due to reduction of transmission.

Conclusions: While there remains much ground to cover for TB control in India, RNTCP's impact over the last two decades illustrates the potential reach of such national, public-sector programmes.

Figure Estimated cumulative lives saved by the RNTCP



PD-977-28 Profile of deaths due to drug-resistant tuberculosis in Brazil, 2013–2015

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Background: The emergence of drug resistant tuberculosis (DR-TB) is one of the major challenges for disease control worldwide. Exposure to previous treatments, inappropriate medication use, treatment default and social determinants may contribute to the occurrence of DR-TB. In 2014, the World Health Organisation (WHO) estimated 190 000 deaths from multidrug-resistant TB. Brazil has low DR-TB incidence rates (less than 3% of new cases); however, a Special Treatment Information System for Tuberculosis (SITE-TB) was fully implemented in 2013 for monitoring DR-TB cases, special treatments and non-tuberculous mycobacteria. This study aimed to describe DR-TB death cases occurred in Brazil in 2013–2015.

Methods: We conducted a descriptive analysis of sociodemographic and clinical variables of laboratory-confirmed DR-TB cases that were registered as death in SITE-TB.

Results: 1013 cases were diagnosed in 2013, of which 6.5% died ($n=66$). Most of death cases occurred among blacks (65.1%), males (65.1%), aged 40–59 years (48.5%), formal and informal workers (62.1%), with 4–7 years of formal education (34.8%) and residents in the northeast of Brazil (48.4%). Concerning to diagnosis and treatment, the most prevalent death rates were registered in new cases (48.5%), under directly observed

treatment (60.6%), with pulmonary forms of TB (92.4%) and the major resistance patterns were multi-drug-resistant (65.0%) and extensively drug-resistant (15.1%). The previous treatment average was three (minimum one and maximum 9). As a result, DR-TB was essentially an acquired condition (86.1%). In addition, 19.1% of death cases were HIV co-infected (approximately 2-fold higher than HIV co-infection rates in drug-sensitive cases). DR-TB treatments lasted on average eight months until death. Drugs associated with higher rates of resistance were rifampicin (78.7%, $n=61$), isoniazid (88.1%, $n=59$), and pyrazinamide (58.8%, $n=17$).

Conclusions: Social determinants such as gender, age and race should be considered by the policy makers. The high percentage of individuals submitted to previous treatments reinforces the importance of monitoring defaulters and the adoption of strategies that enhance treatment adherence and may contribute to the success in TBDR treatment outcomes.

PD-978-28 Analysis of risks factors associated with death in a cohort of tuberculosis patients in Suriname

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Background: Tuberculosis (TB) still causes a substantial number of deaths, especially when complicated by HIV or other comorbidities such as diabetes Mellitus (DM). The Global Tuberculosis Report 2013 showed a more than 3-fold increase in deaths in TB-HIV compared to TB in HIV uninfected. Studies have shown that DM may impact treatment outcome in TB: higher failure rates, higher rates of all-cause mortality, and death specifically related to TB. Preliminary analysis of data shows that nearly one-third of TB patients in Suriname were HIV positive and 10 % has DM.

Methods: This case-control study aims to describe factors associated with death in a cohort of TB patients in Suriname and to analyze their impact on TB treatment outcome. Cases were defined as tuberculosis patients who died during treatment of any cause. Controls were patients who survived with treatment. Lost to follow up were excluded from the study

Results: Having HIV and DM were significantly associated with death (OR for HIV 4.9, χ^2 17.525, $P < 0.05$) and (OR for DM 3.5, χ^2 5.87, $P < 0.05$). The study thus shows that tuberculosis patients who died were more likely to be HIV positive or diabetic. As limitation of this study can be mentioned that smoking and malnutrition were not evaluated because of improper recording of these variables. Further the lost to follow ups could affect the findings, if they died because of TB in reality and were not capture by the surveillance system as such, but classified as lost to follow up. But the findings are similar to studies conducted in this area by others.

Conclusions: HIV and DM have a significantly negative effect on the treatment outcome of TB patients. Based on these findings the NTP must collaborate with the HIV program and chronic care providers to develop adequate integrated strategies to be incorporated into their prevention and control programs. Further analysis is needed to understand the determinants of HIV positive and DM tuberculosis patient that put them at risk to die during treatment.

PD-979-28 Tuberculosis treatment outcomes amongst patients enrolled in treatment with biometric monitoring, India

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Background: Despite recent progress, tuberculosis (TB) remains an important public health problem in India. Individuals in the most deprived socioeconomic groups are at the greatest risk of disease and adverse treatment outcomes. Operation ASHA is a non-governmental organisation which works with national programmes to deliver diagnostics and treatment to India's urban slums and poor rural areas.

Methods: We evaluated treatment outcomes in patients diagnosed through Operation ASHA between April 2012 and September 2014, including demographic information and treatment outcomes. Following diagnosis, all TB patients initiate directly observed therapy (DOT) according to the guidelines of the Revised National Tuberculosis Control Programme. Treatment administration is recorded using a fingerprint-identifying biometric device. Patients were included if they had pulmonary TB with an initial sputum smear result, or extra-pulmonary TB, and were not multi-drug resistant (MDR) at presentation. Outcomes were considered as positive (cured/treatment completed) or negative (treatment failure, default, death, switch to MDR-TB treatment or transfer out).

Multivariable mixed effects logistic regression was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs), adjusted for clustering by treatment centre and Indian state, for the relationships between treatment outcome and age group (≤ 15 , 16–24, 25–44, and ≥ 45 years), sex, previous TB treatment, urban/rural location of treatment centre, and disease type (pulmonary smear-negative, pulmonary low smear-positive [initial smear result scanty or 1+], pulmonary high smear-positive [2+ or 3+] or extra-pulmonary).

Results: 7148/8415 (84.9%) patients had a positive outcome. On multivariable analysis, negative outcomes were more common amongst men (OR = 1.31, 95%CI 1.15–1.51), older patients (OR = 1.12 [1.04–1.21] for each increase in age group) and previously treated patients (OR=2.05 [1.79–2.36]). Compared to smear-negative pulmonary TB patients, patients with extra-pulmonary disease were less likely to have a negative

outcome (OR = 0.72 [0.60–0.87]) whilst pulmonary smear-positive patients were more likely to have negative outcomes (OR = 1.38 [1.15–1.66] and OR = 1.71 [1.44–2.04] for low and high positive).

Conclusions: Despite working with a highly vulnerable population, Operation ASHA's treatment success rate is similar to that reported nationally for India. Men, older patients, retreatment cases and smear-positive pulmonary TB patients may need additional support or further interventions to ensure a positive outcome.

PD-980-28 Recurrence of tuberculosis in a low-incidence setting without directly observed treatment: Victoria, 2002–2014

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Background: Even after tuberculosis (TB) has been successfully treated it can recur. Patients may have recurrent TB of the same strain (relapse) or a new strain (reinfection). It has long been emphasised that treatment adherence plays an important role in preventing the risk of relapse, however several meta-analysis have revealed that directly observed treatment (DOT) does not provide a solution to treatment adherence when compared to self-administered treatment (SAT), and is no better at preventing relapse. There has been a resultant call for research into effective ways to administer TB treatment, to reduce the risk of TB relapse. Victoria, Australia, is an industrialised setting with low TB incidence and universal health care. Individually tailored adherence support for self-administered daily TB treatment is provided. DOT is very rarely used. We aimed to analyse the rate of recurrence in our setting, differentiating, where possible, likely relapses vs. reinfections, and providing transparency regarding the likely treatment adherence of those cases that have relapsed.

Methods: Retrospective cohort study. All recurrent cases of TB were reviewed and 24-loci MIRU-VNTR (mycobacterial interspersed repetitive units-variable number of tandem repeats) molecular typing was used, where possible, to determine the likelihood of relapse or reinfection.

Results: Of 4770 notifications from 2002–2014 (4737 patients), treatment was noted as having been completed in 3987 (96.8%) of 4117 assessable cases, and 26 (0.65%) of these cases experienced recurrence during the study period. Eleven of these cases were culture positive (0.36% of all 3073 culture positive cases): nine were likely relapses (indistinguishable at no more than one of 24 loci) and two were likely reinfections (different at 9 and 16 of 24 loci), giving a TB relapse rate among culture positive cases of 0.051/100 person years of follow up (mean follow-up period of 5.73 years). The median time until relapse was 18 months (interquartile range 12–30

months). Upon recurrence six patients recalled missing doses of medication during their first episode.

Conclusions: Individually tailored adherence support for self-administered TB treatment can ensure good treatment outcomes and treatment adherence that is adequate to achieve low rates of recurrence.

PD-981-28 Long-term risks of repeated tuberculosis treatment episodes in Birmingham, UK

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Background: Repeat episodes of tuberculosis (TB) cause an additional burden on the health system and risk of onward transmission, but we have limited understanding of where they come from and over what time periods.

Methods: We analysed data from a single health facility over 30 years (1980-2011) and linked personal identifiers to recognise repeated individuals treated for TB, rather than asking for self-reported previous episodes of TB. Survival analysis was used to estimate long and short-term risks of repeated TB treatment episodes.

Results: From 10 934 TB disease and 3292 latent TB (LTBI) treatment episodes, repeat episodes occurred in 278/13930 (2%) of individuals. Ascertainment of repeat individuals varied with time. The hazard rate was constant in the first 10 years after the first TB episode and reduced thereafter. Minimum estimates of risk of a repeat TB episode for the first 10 years was 3 per 1000 person-years for recurrent TB disease, 2.8 per 1000 person-years for TB disease after LTBI treatment and 0.6 per 1000 person-years for LTBI treatment after disease or LTBI treatment. Remaining on treatment at 12 months after diagnosis was an independent predictor for recurrent TB disease (adjusted hazard ratio, 6.09; 95% confidence interval, 2.94-12.61; $P < 0.005$).

Conclusions: Patients should routinely be educated about the risk of repeated TB that persists many years after the initial treatment episode. Recording of patient identity and LTBI cases (currently not included in UK surveillance data) are important to quantify the burden of retreatment TB.

PD-982-28 Factors associated with multiple tuberculosis recurrences among HIV-uninfected persons

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Background: HIV is associated with an increased risk of recurrent tuberculosis due to re-infection, presumably because of impaired immunity. Less is known about factors associated with recurrent tuberculosis among HIV-uninfected persons, particularly those who have multiple recurrences. This could provide insights into lack of protective immunity. We hypothesized that factors such as extensive pulmonary disease, extrapulmonary disease, and a shorter time to recurrence are associated with multiple tuberculosis recurrences.

Methods: We included all HIV-uninfected tuberculosis patients from a retrospective cohort seen at a large, urban tuberculosis clinic in Durban, South Africa from January 2000-December 2012, with follow-up through December 2013. Patients whose HIV serostatus changed to positive were excluded. We defined tuberculosis recurrence as a tuberculosis episode occurring after cure or treatment completion of a prior episode. We used a negative binomial regression model to assess factors associated with number of recurrences.

Results: There were 4382 HIV-uninfected patients with 5047 tuberculosis episodes. Of these, 4052 (92%) did not have recurrent tuberculosis, 294 (7%) had a single recurrence, 32 (1%) had two recurrences, and 4 (0.1%) had three recurrences. When adjusting for age and sex, patients with extrapulmonary disease at their first tuberculosis episode had lower recurrence risk than patients with no extrapulmonary disease (incidence rate ratio [IRR] 0.65; 95% confidence interval [CI] 0.46, 0.93; $P = 0.02$). Recurrence risk among patients with cavitary or bilateral disease at their first tuberculosis episode did not significantly differ from those without cavitary or bilateral disease (IRR 1.22; 95%CI 0.98-1.54; $P = 0.08$ and IRR 1.22; 95%CI 0.98-1.51; $P = 0.08$, respectively). Patients with multiple tuberculosis recurrences had significantly shorter median time to recurrence than patients with a single recurrence (3.1 years [interquartile range (IQR) 1.5-4.4] vs. 3.9 years [IQR 2.2-6.7]; $P < 0.001$).

Conclusions: HIV-uninfected patients with multiple recurrences had shorter time to recurrence than those with a single recurrence. Unexpectedly, cavitary and bilateral disease at first tuberculosis episode were not associated with increased risk of recurrences, and extrapulmonary disease was associated with lower recurrence risk. Translational studies may clarify wheth-

er multiple tuberculosis recurrences are related to impaired immunity.

PD-983-28 Determinants of mortality due to tuberculosis in Amazonas, Brazil: a challenge for the End TB strategy

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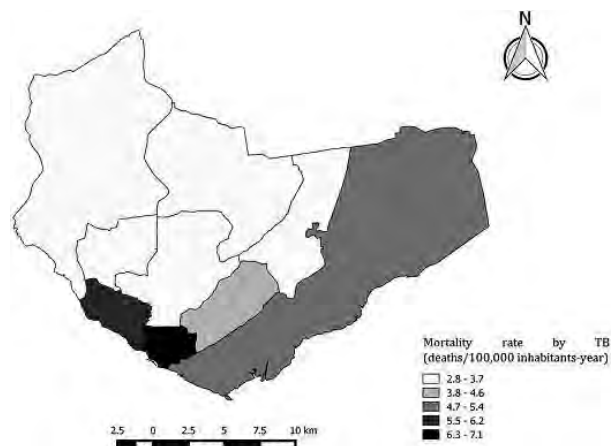
Background: In 2014, the World Health Assembly approved the strategy end TB, an ambitious target. The aim is to end the global TB epidemic, with targets to reduce TB deaths by 95% and to cut new cases by 90% between 2015 and 2035, and to ensure that no family is burdened with catastrophic expenses due to TB. Brazil, which figures on the list of 22 countries that concentrate 80% of global TB cases, ranking 16th, reveals great challenges to reach that target, especially in Amazonas. Therefore, the objective is to analyze the determinants of mortality by TB in the capital of Amazonas and thus verify the spatial distribution of deaths in that region.

Methods: Ecological study that considered deaths between 2006 and 2014, processed in the Mortality Information System (SIM), whose basic cause lists all clinical forms of the disease according to the International Classification of Diseases version 10 (ICD10) from A15 till A19.9. The mortality rates by TB (deaths/100 000 inhabitants-year) were calculated and analyzed according to some determinants: sex, education, occupation, marital status and area of residence. Thematic maps were constructed according to sub-districts of the urban region of Manaus, using the software Quantum GIS (QGIS).

Results: Six hundred deaths due to TB were identified. As for the determinants of mortality, a median age of 56 years was determined, male sex ($n = 463$; 77.17%), mulatto ethnic origin ($n = 445$; 74.17%), secondary education ($n = 124$; 20.67%) and marital status single ($n = 213$; 35.5%). Concerning the spatial distribution of the mortality rate, four sub-districts showed higher coefficients than the city (3.7 deaths/ 100 000 inhabitants-year), the highest coefficient was found in the Southern sub-district (7.08 deaths/100 000 inhabitants-year) and the sub-district with the lowest mortality rate was the North (2.89 deaths/100 000 inhabitants-year) (Figure).

Conclusions: The study revealed the male sex, productive age, average education and mulatto ethnic origin as the determinants of mortality by tuberculosis, indicating that Brazil faces many difficulties to achieve the World Health Organization (WHO) ambitious target of putting an end to TB.

Figure Distribution of mortality rates by TB



PD-984-28 Late commencement of anti-tuberculosis drugs in three DOTS referral centres in Benue State, Nigeria: a neglected correlate of tuberculosis management

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Background: Most research on the correlate of tuberculosis (TB) treatment outcomes place emphasis on socio-demographic characteristics of the patients, Human Immunodeficiency Virus status and CD4⁺ count of patients and nutrition among others. This study assessed the effect of delay in commencement of anti-TB regimen on the treatment outcomes of all TB patients treated between 2011 and 2014 in three high burden TB, DOTS centres in Benue State, Nigeria.

Methods: A retrospective cohort study with convenient sampling technique was used for all registered Tuberculosis patients enrolled for treatment within the reviewed period. Instruments for data collection were standardized facility reporting registers and patients treatment cards. The χ^2 test was used for test of association between the independent variables and the main outcomes of the study, with statistical significance set at $P = 5\%$.

Results: Of the total 1711 cases reviewed, the males to females ratio was 3.9:1. The mean age for the male patients was 39.0 ± 15.3 years and the females 33.7 ± 14.2 years. Majority of the patients were new pulmonary Tuberculosis cases and they commenced their treatment after three weeks of diagnosis. Higher failure and death rate were reported amongst the patients who commenced their treatment late (78.7% and 42.5% respectively). The relationship between the treatment outcome and the time of commencement of anti-TB drug regimen was statistically significant ($P = 0.000$).

Conclusions: With the current upsurge of multi-drug resistant TB in the country, early commencement of anti-TB drugs in all diagnosed TB patients is an important correlate that must be addressed in order to achieve the global goal of reducing TB prevalence to the level at which it will no longer constitute a public health problem in Nigeria.

38. Alternative diagnostics: from biomarkers, serology to X-ray

PD-985-28 The diagnostic value of immunologic tests in differential diagnosis of infiltrative pulmonary TB

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Background: To evaluate the diagnostic value of the combined use of immunologic skin tests in differential diagnosis of infiltrative pulmonary TB.

Methods: We analyzed test data obtained from 181 patients with the diagnoses verified at the Central TB Research Institute as follows: infiltrative pulmonary TB ($n = 48$), community-acquired pneumonia ($n = 41$), lung cancer ($n = 34$), hypersensitivity pneumonia ($n = 25$), pulmonary sarcoidosis ($n = 33$). They were 92 males (50.8%), and 89 females (49.2%). Their age ranged from 17 to 100 years. We performed the Mantoux test with 2 TU PPD-L, the Diaskintest[®] (skin test using recombinant TB allergen), and the QuantiFERON[®]-TB Gold.

Results: Practically all the patients with infiltrative pulmonary TB had positive reactions to the Mantoux test with 2 TU PPD-L (87.5%); the other patients had positive reactions to this test reliably less frequently: community-acquired pneumonia - 68.7%, lung cancer - 61.8%, hypersensitive pneumonia - 28%, pulmonary sarcoidosis - 12.1%. We established that the combined use of the immunologic skin tests (the Mantoux test with 2 TU PPD-L and the Diaskintest allowed narrowing diagnostic search. A positive reaction to the Mantoux test with 2 TU PPD-L accompanied by a negative reaction to the Diaskintest were more frequent in patients with pneumonia, lung cancer or lung diseases. The results of the QuantiFERON-TV Gold demonstrated complete matching to both positive and negative results of the Diaskintest, which would allow using the test in vitro in cases of contraindications to the skin test.

Conclusions: The combined use of the tests (the Mantoux test with 2 TU PPD-L and the Diaskintest) allowed significantly narrowing diagnostic search. Matching of the QuantiFERON-TV Gold and Diaskintest results determined the possibility to perform the test in vitro, if there were any contradictions to skin testing.

PD-986-28 Performance of gene expression signatures in the context of intensified tuberculosis case finding among people living with HIV

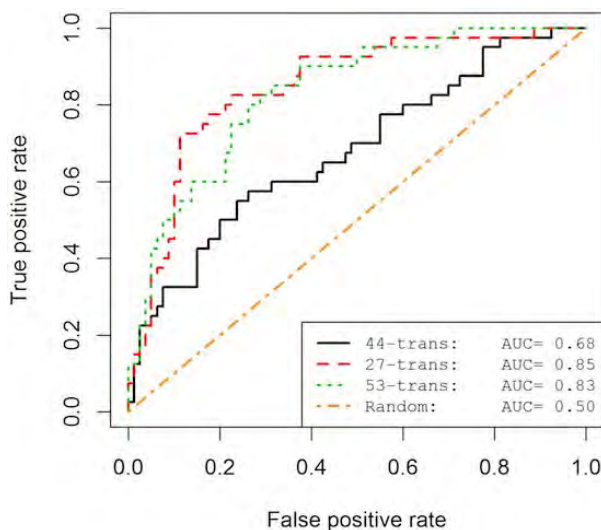
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Background: Host blood gene expression signatures are being explored as a way to improve TB diagnosis, but have not been evaluated in the context of intensified case finding (ICF) among PLHIV.

Methods: From 07/2013-04/2015, we enrolled 665 PLHIV with CD4 cell counts ≤ 350 cells/ μ l presenting to the Mulago AIDS Clinic (Kampala, Uganda) for antiretroviral therapy initiation. All participants underwent comprehensive TB testing including sputum mycobacterial culture x2. We considered patients to have active TB if *Mycobacterium tuberculosis* was isolated from ≥ 1 sputum culture; TB was excluded if both cultures were negative. For this nested case-control study, we included 40 consecutive participants with culture-confirmed TB as cases. Two controls were matched to every case by study enrollment date. RNA from whole blood collected at enrollment was used to determine normalized gene expression levels (Illumina HumanHT-12 v4 Beadchip). We calculated the Disease Risk Score (DRS) for 27-, 44-, and 53-transcript signatures reported previously to distinguish active TB from LTBI, other diseases and LTBI/other diseases, respectively. We performed receiver operating characteristic (ROC) analysis to assess the diagnostic accuracy of each signature.

Results: Of 120 participants, 61 were female, median age was 33 and median CD4 cell count was 156. Area under the ROC curve was 0.85, 0.68, and 0.83 for the 27-, 44- and 53-transcript signatures, respectively (**Figure 1**). When maximizing overall accuracy, sensitivity and specificity of the 27-, 44- and 53-transcript signatures were 75% and 83.4%, 60% and 62.5%, and 75% and 77.5%, respectively. By comparison, the sensitivity and specificity of the inflammatory marker C-reactive protein were 82.5% and 80%, respectively.

Conclusions: The best performing gene expression signatures published to date did not meet the WHO-recommended sensitivity/specificity thresholds for a biomarker-based TB screening or diagnostic test. Further work is required to identify more robust signatures for use in the context of ICF.



PD-987-28 Evaluating the effect of T-Cell Xtend on T-SPOT.TB assay results

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Background: T-SPOT.TB (TSPOT) is an interferon-gamma release blood assay (IGRA) for latent tuberculosis (TB) infection (LTBI). Results are determined by counts of sensitized effector T cells. Delays in sample processing reduce IGRA sensitivity. Because samples in the USA are generally processed at a central laboratory in Memphis, shipment over long distances may take a day or longer, potentially affecting the assay's accuracy. The manufacturer, Oxford Immunotec (OI), has developed a reagent, T-Cell Xtend, that is added at the time of processing; it removes granulocytes from the peripheral blood mononuclear cell (PBMC) layer. According to OI, this allows the T-SPOT assay to be performed on blood samples stored up to 32 hours without compromising accuracy. Although several studies have examined the issue, it remains unclear whether Xtend prolongs sample viability.

Methods: The Tuberculosis Epidemiologic Studies Consortium's long-term cohort study is evaluating the predictive value of the three available tests for LTBI in high-risk populations. A subset of participants in Hawaii had paired TSPOT samples processed in the local state laboratory. The samples were processed in three groups; in each group, Xtend was added to one of the paired samples. Group 1 samples ($n=51$) were sent to the laboratory within four hours after collection and Group 2 samples ($n=57$) were stored overnight at room temperature. In Group 3 ($n=53$), one of the paired samples was held overnight at room temperature, then

processed using T-Cell Xtend; the other was sent to the laboratory immediately and processed without T-Cell Xtend. The results were analyzed using χ^2 and paired t -tests.

Results: Paired samples from Groups 1 and 2 showed no difference in categorical results or mean number of spots. Samples in Group 3 showed no difference in the categorical results, but the mean number of spots was significantly lower in those samples treated with Xtend (5.64 vs. 7.2, $P < 0.05$).

Conclusions: The addition of T-Cell Xtend does not seem to enhance the TSPOT results with delayed processing. Enrollment of additional subjects is needed to confirm this finding.

PD-988-28 Identification of novel host biomarkers in plasma as candidates for the immunodiagnosis of tuberculosis disease

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Background: There is an urgent need for new tools for the rapid diagnosis of tuberculosis (TB) disease, and monitoring of the response to treatment. Immunodiagnostic approaches might be beneficial, especially if based on the detection of host biomarkers in easily available samples such as serum or plasma, as they may be easily adaptable into point-of-care tests. The aim of the present study was to identify such candidate biomarkers

Methods: We recruited 22 TB patients and 33 individuals with signs and symptoms suggestive of TB, but in whom TB disease was ruled out, at a health centre in Cape Town, South Africa. Using a multiplex platform, we evaluated the levels of 74 host biomarkers in plasma samples from these individuals, as candidates for the diagnosis of TB disease or monitoring of the response to treatment.

Results: The concentrations of 23 host markers were significantly different between the TB patients and individuals with other respiratory diseases (ORD), as determined by the Mann Whitney U test. The most accurate single host markers included CRP, SAP, IP-10, NCAM, ferritin, TPA, I-309, and MIG, which diagnosed TB disease with area under the ROC curve ≥ 0.80 . However, the optimal diagnostic biosignature was a combination of NCAM, SAP, IL-1 β , sCD40L, IL-13 and APO A1, which diagnosed TB disease with a sensitivity of 100% and specificity of 89.3% after leave-one-out cross validation. When compared to baseline levels, the concentrations of 11 host markers were significantly different at the end of TB treatment, thereby indicating that they may be potentially useful in monitoring of TB treatment response.

Conclusions: We have identified candidate host biomarkers which may be useful in the diagnosis of TB disease and monitoring of the response to TB treatment. Our findings require further validation in larger studies.

PD-989-28 Equal sensitivity of the new generation QuantiFERON®-TB Gold plus in direct comparison with the previous version, QuantiFERON-TB Gold IT

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Background: Rapid and reliable identification of individuals latently infected with TB bacteria (LTBI) as well as of patients with active disease (aTB) is crucial in order to efficiently control the worldwide TB epidemic. QuantiFERON-TB Gold in tube (QFTG-IT) is an immunologic assay analyzing interferon-gamma (IFG) released from CD4⁺ T-cells after stimulation with specific TB antigens. The assay is widely used for LTBI and TB diagnostics though it suffers from a relatively low sensitivity of approximately 80%. Now, Qiagen has released a new test generation (QFTGplus) which also analysis the response of CD8⁺ T-cells in a separate TB2-test tube and campaigns with significantly higher sensitivity.

Methods: We investigated both test generations in a direct head to head comparison. Lithium heparin blood samples of study participants were simultaneously inoculated in both QFTG-IT and QFTGplus latest three hours after collection. Tests were strictly handled according to the instructions of the manufacturer.

Results: Among 163 study participants, 77 were health care workers (HCW) and 86 presumed TB cases of whom 57 had a final diagnosis of TB. Identical sensitivity rates of 89.5% (95%CI 81.5–97.5) for the diagnosis of aTB were observed for both test generations. The positivity rates of QFTG-IT and QFTGplus were 10.4% (95%CI 3.6–17.2) and 13.0% (95%CI 5.5–20.5), respectively, for HCW (χ^2 2-tailed, $P = 0.8$), and 27.6% (95%CI 11.3–43.9) and 33.3% (95%CI 16.2–50.5), respectively, for non-TB patients. All discrepantly positive results had IFG values near the cut-off. Mean IFG concentrations were higher in QFTG-IT than in the new test generation, only around the cut-off QFTGplus yielded slightly higher values.

Conclusions: Sensitivity of QFTGplus was identical to QFTG-IT in direct comparison. Whether the slightly higher positivity rates of QFTGplus among non-TB subjects and HCW have been triggered by an increase in sensitivity for LTBI detection or by an increase of the false positive rate needs to be further investigated.

PD-990-28 Evaluation of the antibody in lymphocyte supernatant assay in the detection of active tuberculosis

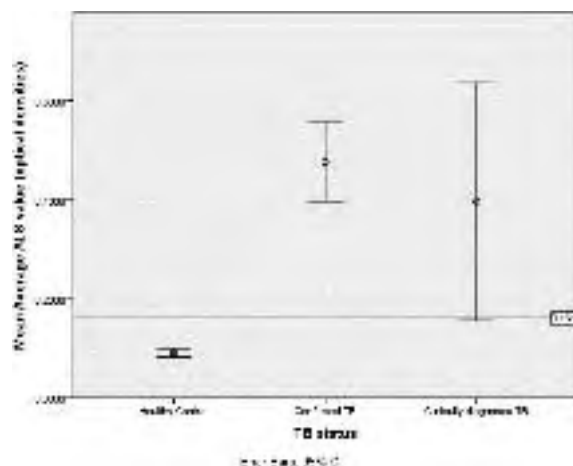
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Background: Immune responses to tuberculosis (TB) may be used as biomarkers of disease activity. The Antibodies in Lymphocyte Supernatant (ALS) assay measures pathogen-specific immunoglobulin G (IgG) secretion from activated plasmablasts that are transiently found in circulation. We hypothesize that the ALS assay can be used as an alternative method to support the diagnosis of TB, and may be especially helpful among patients who are unable to produce sputum.

Methods: Adults presenting to Kibong'oto National Tuberculosis Hospital with suspicion for pulmonary TB were recruited. GeneXpert and mycobacterial culture were used to confirm the diagnosis. Patients were categorized as having confirmed- or clinically-diagnosed TB. Patients with no prior TB history and no current symptoms of TB served as healthy controls. Peripheral blood mononuclear cells were isolated from participants and cultured unstimulated for 72 hours. Secreted antibodies were detected by enzyme-linked immunosorbent assay (ELISA) using Bacille-Calmette Guerin (BCG) vaccine as the coating antigen. Mean ALS values were compared between TB cases and controls.

Results: We recruited 74 confirmed TB cases (27 MDR-TB, 13 retreatment, 34 drug-sensitive), 11 clinically diagnosed TB cases, and 28 healthy controls. Compared to the healthy controls, the mean ALS values were highest among patients with confirmed TB at $0.477 + 0.342$ ($P < 0.001$, Figure). Patients with clinically diagnosed TB had mean ALS values of $0.397 + 0.357$. Among the 11 clinically diagnosed TB cases, 10 (91%) had values above the cutoff for a positive test (0.161). Using a composite reference of TB culture and/or GeneXpert MTB/RIF test positivity, the sensitivity of ALS was 87.8% and specificity was 18.2%.

Conclusions: ALS identified more cases of TB as compared to culture/GeneXpert. These results suggest that BCG-specific IgG-secreting peripheral plasmablasts activity may be used as a diagnostic biomarker, particularly in people who are not able to produce sputum of good quality.



PD-991-28 Multidrug-resistant mycobacterial strains in lymph node aspirated specimens from a National Reference Laboratory in India

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Background: The increasing incidence of extra pulmonary TB has been reported world over irrespective of economic status of countries. Among various forms of extra pulmonary tuberculosis, the incidence of tuberculous lymphadenitis has increased in parallel to mycobacterial infection ubiquitously. The findings on susceptibility pattern of mycobacteria isolated from lymph node specimens is need of the hour, which would aid the National TB Control Program. The aim of the study was to determine the frequency and pattern of drug resistant *M. tuberculosis* isolates among TB lymphadenitis patients from a tertiary care centre.

Methods: The yearlong study was undertaken in the Department of Microbiology from January-December, 2014. All patients with swelling of superficial cervical lymph nodes were subjected for fine needle aspiration (FNA) using 10 ml syringe fitted with 21 G needle. The aspirated samples were collected in sterile Mc Cartney bottles and immediately transported to the Microbiology laboratory. Samples were processed in the BSL III laboratory by NALC - NaOH method for smear examination and culture. Culture and susceptibility testing was performed in an automated mycobacterial culture and susceptibility testing system MGIT 960.

Results: In the study 154 lymph node samples were processed, i.e. 39.28% of 392 extra pulmonary specimens. 100/154 (64.93%) cases were female and 54/154 (35.06%) were male. patients' samples were clinically categorised as failure (60/154, 38.96%), new (49/154, 31.81%), relapse (37/154, 24.02%), defaulter (4/154, 2.59%), chronic (3/154, 1.94%) and unknown (1/154, 0.64%). Of the 154 samples, 26 cultures (16.88%) were positive for AFB, of which 92.30% (24/26) were identified as *M. tuberculosis* complex and 7.69% (2/

26) was nontuberculous mycobacterium. The susceptibility analysis of 24 positive cases showed that 7/154 (4.54%) were sensitive to all four first-line drugs whereas (15/154; 9.74%) strains were multidrug-resistant. Within the MDR strains, it was observed that (3/49; 6.12%) were from new and (12/105, 11.40%) were from retreatment cases. Altogether 6 different susceptibility patterns were observed.

Conclusions: Multidrug-resistant tuberculous lymphadenitis is an emerging health problem in India. Findings highlight the importance of doing susceptibility testing and identifying MDR strain in a patient of lymph node tuberculosis for appropriate treatment and management.

PD-992-28 Utility of urine lipoarabinomannan in diagnosing tuberculosis and predicting mortality with and without HIV: an Asian perspective

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Background: Early diagnosis and treatment is a key factor to reduce mortality rate in disseminated tuberculosis (TB), especially among immunocompromised host and advanced HIV. However, it is difficult to obtain sufficient clinical specimen and sputum in these patients. Measuring lipoarabinomannan (LAM) in urine is simple and maybe promising in diagnosing disseminated TB. This study evaluated the applicability and accuracy of urine LAM test among TB-HIV co-infected, non-HIV-infected and non-HIV-infected immunocompromised patients.

Methods: Baseline frozen urine samples with proven culture-positive TB from our TB research cohort were selected for blinded urine LAM testing. 109 patients were categorized into 4 groups:

1) HIV-infected patients with TB; 2) non-HIV-infected patients with disseminated TB; 3) non-HIV-infected immunocompromised patients with TB (non-disseminated TB); and 4) healthy individuals with no active TB. Sensitivity in patients with culture-positive TB and specificity in patients without TB, positive predicted value (PPV) and negative predicted value (NPV) were assessed.

Results: The sensitivity of the urine LAM test in group 1 for CD4 T-cell counts >100 , ≤ 100 and ≤ 50 cell/mm³ were 38.5%, 40.6% and 45%, respectively. The specificity and PPV were more than 80%. In groups 2 and 3, the sensitivity of the test was 28.6% and 10%, respectively, and the specificity and PPV were 100% for both groups. In addition, positive urine LAM in HIV patients with active TB significantly associated with

death (25% vs. 3.7% in urine LAM positive vs. negative patients; $P=0.02$). In TB-HIV co-infection patients who had $CD4 \leq 50$ cell/mm³ and urine LAM positive, the mortality rate was as high as 50%.

Conclusions: The findings support the potential role of urine LAM test in Asia to improve the diagnosis of disseminated TB among HIV-infected, non-HIV-infected, and non-HIV-infected immunocompromised patients with disseminated TB. Moreover, it may predict the risk of mortality among HIV-infected patients with TB.

PD-993-28 Chest X-ray findings in tuberculosis patients identified by spot sputum culture screening

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Background: Screening for tuberculosis (TB) in high-risk groups in low-incidence countries is recommended by the World Health Organization. Spot sputum culture (SSC) screening is a novel screening approach and may be more sensitive than mobile x-ray screening.

Aim: To investigate whether changes suggestive of tuberculosis (TB) were present on chest x-rays (CXR) from TB patients identified by SSC screening, indicating that SSC screening and CXR screening are equally sensitive.

Methods: CXRs from 39 culture-positive patients, identified by SSC screening in Copenhagen from 2012-2014, were included in the study. These chest x-rays, 39 normal CXRs from persons screened by mobile x-ray, and 39 chest X-rays from culture-positive TB patients not identified by screening (controls) were anonymised and put into random order. Two respiratory physicians and two radiologists read the CXRs and classified the findings as normal or abnormal, acute and/or chronic, followed by a sub-categorisation.

Results: Abnormalities (all) were identified in 77.6% (mean, SD = 9.1, range = 64.1%-87.2%) of the SSC screening group and 95% (mean, SD = 2.9, range = 90%-96.7%) of the control group. Abnormalities classified as acute were identified in 61.9% (mean, SD = 11.9, range = 51%-82%) of the SSC screening group and 78% (mean, SD = 11.1, range = 60%-90%) of the control group. Abnormalities suggestive of TB were identified in 38.1% (mean, SD = 8.4, range = 30.8%-51.3%) of the SSC screening group, and 60.2% (mean, SD = 5.9, range = 50%-64.3%) of the control group.

Conclusions: Chest X-ray may be normal in TB patients identified by SSC screening, therefore SSC screening may be a more sensitive approach.

ABSTRACT PRESENTATIONS SATURDAY 29 OCTOBER 2016

e-POSTER SESSIONS

10. Eyes, ears and kidneys: MDR drug toxicity

EP-186-29 Ascertaining the proportion of sensory neural hearing loss among MDR-TB patients placed on kanamycin using pure tone audiometry

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Setting: The emergence of drug resistance TB is a major challenge to global TB control. Treatment of MDR-TB has been problematic and the side effects of most of the drugs have been challenging and intolerable. According to Katzung (2007) ototoxicity can manifest itself either as auditory damage; Resulting to tinnitus and high frequency hearing loss, initially or as vestibular damage, evidenced by vertigo, ataxia and loss of balance. Pure tone audiometry (PTA) is the key hearing test used to identify hearing threshold levels of an individual, enabling determination of the degree, type and configuration of a hearing loss.

Justification: With increasing ototoxic side effect of aminoglycosides in the treatment of MDR-TB in Nigeria it became imperative to, conduct pure tone audiometry of MDR-TB patients on before Treatment. To compare the audiometry findings prior and different stages of MDR-TB treatment. To determine the effect of aminoglycosides on cochlear and vestibular functions, cochlear and vestibular dysfunction.

Methodology: History and examination with emphasis on ENT and previous exposure to any cause of hearing loss were carried out. Prior to the test all the patients had otoscopy and external auditory canal cleared of wax or debris where applicable. After being given information about the testing in the language they understood, the test was conducted in accordance with British Society of Audiology (BSA) recommendation. Hearing threshold, 25Db or less were regarded as normal. Normal hearing 0-25db, Mild hearing loss 26-40db, Moderate hearing loss 41-

55db, Moderate severe hearing loss 56-70db and Severe Hearing loss 70-91db.

Result: Out of 100 MDR-TB patients started on treatment, 38 (38%, *P*-value 0.01) had various degree of hearing impairment. (Mild Sensory Nerve Hearing Loss to Profound Sensory Nerve Hearing Loss). 62% had normal hearing after initiation of treatment. However (9%) had mild bilateral Sensory Nerve hearing loss prior to initiation of treatment.

Discussion: The audiometry assessment is necessary prior to initiation of any patients on aminoglycosides. The National TB control program should consider switching over to capreomycin with milder side effects or introducing drugs with shorter regimen.

EP-187-29 Screening for aminoglycoside ototoxicity among patients receiving treatment for MDR-TB: preliminary results of the first Ethiopian audiology screening program

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Background: An estimated 10-20% of patients receiving aminoglycoside or polypeptide injectable (AG) therapy for multidrug resistant tuberculosis (MDR-TB) experience irreversible sensorineural hearing loss. Guidelines recommend audiometry screening during intensive phase therapy to prevent ototoxicity; however, lack of training and equipment limit testing in low resource settings. Current detection relies on subjective patient report. Our goal was to assess the feasibility of implementing an audiology screening program at an MDR-TB referral hospital in Ethiopia.

Methods: This is a prospective pilot study in which MDR-TB patients at St. Peter's Tuberculosis Specialized Hospital in Addis Ababa were included if: > age 18, they received ≤ 3 doses of prior 2nd-line AG therapy, and they provided informed consent. Patient history, otoscopy and pure-tone threshold audiometry (125-8000Hz) were completed at baseline and monthly follow-up during AG treatment. Hearing loss was defined by the American Speech-Language Hearing Association Guidelines (1994). De-identified patient data was stored in secure iPad application and database.

Results: 49 patients were enrolled aged 18-60. Twenty-one (43%) were female. All patients are currently receiving capreomycin (Cm). Sixteen (33%)

were previously treated with streptomycin. Four patients (8%) had subjective hearing loss at baseline and 10 (20%) at a follow up. Fourteen patients (29%) had abnormal otoscopy including impacted cerumen and perforated tympanic membranes (5 patients). Audiometer detected hearing loss was found in 11 patients (22%) of whom 2 received prior streptomycin, and 5 had subjective hearing loss. Three patients (6%) were thought to have injectable induced hearing loss. All had renal dysfunction (creatinine nearly doubled from baseline) and all had Cm injections decreased from 6 to 3 times per week due to hearing loss and impaired renal function.

Conclusions: We demonstrate that audiology screening improves clinical decision making by providing an objective assessment of hearing loss in this MDR-treatment cohort from Ethiopia. We also show a poor correlation of patient-reported hearing loss with audiometer results. We speculate that the low incidence of AG-induced hearing loss may be related to the use of less ototoxic Cm. This pilot program demonstrates that it is feasible to implement audiology screening during injectable MDR-TB treatment in low resource settings.

EP-188-29 Incorporating mobile automated audiometry into MDR-TB patient treatment plans

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Among the powerful agents used to treat multidrug-resistant tuberculosis (MDR-TB), aminoglycosides can be effective in treating life-threatening pathogens, but can also have irreversible toxic effects on key physiological functions. Drugs that are toxic to the inner ear and hearing are known as ototoxic, and aminoglycosides are notorious ototoxic agents. To help determine the noxious effects of ototoxic agents, hearing thresholds can be monitored during MDR-TB treatment. Challenges here include the fact that hearing testing has historically been limited to be performed by trained hearing specialists as well as requiring sound booths. Both of these elements are rare in the developing world. Automated mobile audiometry with integrated ambient noise monitoring has recently become available. The automated functionality of these systems does not require in-depth audiological training, and the ambient noise monitoring combined with the use of specific headphones allows for clinically valid hearing testing outside of a sound chamber. The methods and considerations for use of this type of testing will be presented. Two separate, multi-site, MDR-TB clinical trials are currently using mobile automated audiometry systems; with testing sites in 7 developing countries and counting. The total number of patients tested, as well as learned implementation strategies

and obstacles will be presented. Clinically valid mobile automated audiometry is now a feasible and effective tool for measuring and contrasting hearing thresholds in the developing world.

EP-189-29 Improving the monitoring of ototoxicity among DR-TB patients receiving aminoglycosides in South Africa

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Background: DR TB Patients presenting with hearing loss is a prevalent adverse event caused by the administration of aminoglycosides. Therefore access to audiology services before and during treatment is imperative to prevent hearing loss. With only 461 Audiologists in the Public Sector in South Africa, it is difficult to provide hearing tests for all DR-TB patients. Delay in testing and inadequate monitoring of ototoxicity were observed during DR-TB treatment. This paper aims at providing an account with regards to the 125 portable audiometers deployed to increase the access to audiology services among DR-TB patients in South Africa.

Intervention: One hundred and twenty five (125) high frequency portable audiometers with auto-interpretation capability were deployed between the year 2012 and 2015 at various health care facilities in South Africa to improve the monitoring of ototoxicity among DR-TB patients. All end users were trained on how to use the devices. The automated programme, is user friendly for both mid-level workers and professional staff. The device is portable and compact and therefore convenient to move around, which improves the accessibility of the service. The data generated from the audiological tests are uploaded to a Central Connect Server. An online interpretation report is generated and a SMS or email notification of the interpretation results are sent to the relevant clinicians'. As soon as a network connection is available, the clinical data is synchronised through a secure socket layer connection to an eHealth Cloud. The data is collected in the server database from where reports can be generated and viewed over the internet.

Results: The data entry from January 2015- February 2016 indicated that 2583 patients were screened for ototoxicity using the high frequency audiometer. Of the 2583, 24,08% presented with an initial hearing loss, of which 11% had a slight hearing loss (26-40 dB), 6% moderate (41-60dB), 4%, severe (61-80Db) and 6%, profound >80 Db . 7% (n=2583) of the patients presented with ototoxicity.

Conclusion: The intervention facilitates the early identification of ototoxicity and associated risk factors that creates an opportunity for the adjustment

of clinical management in order to conserve the hearing of DR- TB patients.

EP-190-29 Symptom and laboratory screening for early detection of ototoxicity among registered DR-TB patients in Delhi, India

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Introduction: Despite commendable advancements made towards control of drug resistant Tuberculosis (DRTB), a sizable number of treated patients report inability to adhere to their treatment protocol. Researchers have posited that apart from the polemics of regimen efficacy, addressing severe adverse drug reactions is an important determinant for treatment compliance. Ototoxicity is one of the severe adverse drug reactions which if not managed timely, results in irreversible hearing loss among those on aminoglycosides treatment in DRTB management. The study aims to highlight the need for baseline and continuous symptomatic and lab screening of hearing disability for early detection of ototoxicity among DRTB patients registered in Delhi.

Methodology: All the DRTB patients registered at DRTB management center of the Revised National Tuberculosis Control program in Central Delhi for the period 2012-2015 were enrolled in the study. Baseline Audiometric evaluation was done for all registered patients. Checklist based symptomatic screening for hearing disability was done by the paramedical staff daily, at the peripheral treatment centers. Symptoms graded for lab evaluation were then referred to Audiometry Lab at the DRTB Centre. Recording of all patients found to have Ototoxicity based on Otorhinolaryngology evaluation was done for the study period. Significance of severe adverse drug reaction with duration of therapy was analysed on SPSS 16.

Result: In the study period, 1563 DRTB patients were registered for DRTB treatment at the DRTB centre. All were subjected to baseline Audiometric evaluation. It was observed that 5% (85) patients had Audiometric errors reported significant enough to stop or discontinue the offending drug (Kanamycin) during their DRTB treatment. On symptomatic screening for hearing disability, more than half 51% (43/85) had audiometric errors reported and drug was stopped/ discontinued due to ototoxicity. The toxicity was associated significantly with early months (month1 and 2) of therapy ($P < 0.05$ levels).

Conclusion: For patients registered on DRTB treatment with aminoglycosides (kanamycin), continuous monitoring for ototoxicity as a severe adverse drug

reaction is needed to ensure treatment compliance and quality care in high workload settings.

EP-191-29 Evaluating the impact of adverse drug reactions and application of second-line anti-tuberculosis drugs

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Background: The first-line anti tuberculosis (TB) agents recommended by WHO includes isoniazid, rifampin, pyrazinamide and ethambutol. However, in the setting of drug resistance and intolerance to adverse drug reaction, second-line TB drugs are another alternative treatment option. The use of second-line anti-TB drugs are monitored by Taiwan CDC since 2006, in order to avoid progression into drug resistance due to inadequate treatment regimen, second-line anti-TB drugs application forms must be submitted by physicians prior prescribe such drugs. The aims of this study were to investigate the adverse drug reactions (ADR) from first-line anti-TB drugs and alternatives of the second-line anti-TB drugs application.

Methods: A retrospective study of adverse drug reactions was conducted from January 2010 to December 2014 in Central Taiwan. Drug resistance tuberculosis patients were excluded. 620 cases out of 1140 second-line Anti-TB drugs applications were enrolled. Symptoms of adverse drug reaction and selection of alternative drug was evaluated by physician and verified by Taiwan CDC. Adverse drug reactions were classified by international medical terminology dictionary MedDRA.

Results: 11,292 cases diagnosed with tuberculosis in central Taiwan and 482 cases with adverse drug reaction, 68.9% were male, median age were 69.1 years old. 87 cases experienced at least one adverse drug reaction. Liver related disorders were the most common reason for applying second-line TB drugs with 70.1% of adverse drug reaction followed by 23% of skin disorders. In alternative of second-line drugs application, 70.3% used oral fluoroquinolones (FQ) and 4.4% injectable aminoglycosides, 11.6% concomitant oral FQ and injectable aminoglycosides. 61.2% application cases were cured or completed treatment after receiving alternative anti-TB drug therapy.

Conclusions: There were 4.28% of TB cases received second-line anti-TB drugs due to intolerance to adverse drug reaction from first-line anti-TB drugs in central Taiwan. Drug-induced liver injury was a major complication in first-line anti-TB drug. Hepa-

totoxicity and skin allergy was the most common adverse drug reactions, thus led to second-line anti-TB drugs applications. Oral fluoroquinolones were the major second-line anti-TB drugs choice when intolerant to adverse drug reaction occurred.

EP-192-29 Avoiding nephrotoxicity during treatment of multidrug-resistant tuberculosis by stepwise extension of aminoglycoside dosing intervals

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Background: Aminoglycoside is one of the key elements for treatment of multidrug resistant tuberculosis (MDR-TB). However, intensive aminoglycoside treatment may cause disabling nephrotoxicity.

Methods: Patients with documented MDR-TB were treated according to the current World Health Organization (WHO) guidelines. The dosing frequency of aminoglycoside were initially once daily and gradually tapered to thrice or twice weekly. Directly Observed Therapy (DOT) was administered throughout the whole treatment course by trained treatment supporters for all patients. Renal function was monitored monthly. Nephrotoxicity was defined as increment in serum creatinine level of 1mg/dl or 2 times of baseline level.

Results: From Jan to Dec 2013, 44 patients (31 males, mean age 58.4 years) were treated according to the protocol. Resistance to fluoroquinolones was detected in 6 (13.6%). Sputum mycobacterial culture conversion occurred at a median of 34.5th day after start of treatment. The mean treatment duration was 20.7 months with a cure rate of 88.6%. Two patients (4.5%) died during the treatment course, two patients lost to follow up and one patient experienced treatment failure. Aminoglycoside was administered to all patients with a mean dosage of 12.5mg/dl. Kanamycin, streptomycin, and capreomycin were used in 42, 1, and 1 patients, respectively. The overall duration of aminoglycoside administration was 209 days in average. The mean duration of each dosing frequency of aminoglycoside was 34.3 days, 42.9 days, 39.0 days, and 84.7 days for daily, five times weekly, thrice weekly, and twice weekly, respectively. Baseline renal function impairment was noted in one patient. Only one patient (2.3%) developed transient nephrotoxicity and recovered completely.

Conclusions: With comprehensive DOT program, the WHO guideline-based regimen is highly effective for

MDR-TB. Using a stepwise extension of aminoglycoside dosing interval, the risk of nephrotoxicity can be minimized.

EP-193-29 Adverse events associated with short-course treatment of multidrug-resistant tuberculosis in Niger: 5 years of experience

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Background: Outcomes in patients treated with short regimens for MDR-TB are encouraging. However limited experience exists about drug-associated adverse events (AEs).

Methods: The study was observational and retrospective. Case records of confirmed MDR-TB patients enrolled between July 2008 and September 2013 on a 9 to 14-month standardized regimen were analysed. The regimen was composed of kanamycin, high doses of gatifloxacin, prothionamide, clofazimine, medium-high doses of isoniazid, ethambutol and pyrazinamide. Cohort Event Monitoring was used. Events were graded according to severity (grade 1= mild; 2= moderate; 3= severe, drug stopped; 4= life-threatening or permanently disabling).

Results: Among the 122 patients included, 101 (82.8%) were males; the median age was 30 and the median BMI was 16.4 kg/m² (IQR: 14.8-19). One hundred fifteen (94.3%) patients underwent an HIV test and 6 (5.2%) were positive. One hundred eleven AEs were experienced by 81/122 (66.4%) patients. The majority of them ($n=72$; 88.9%) had mild to moderate AEs and in 9 cases (11.1%) they required to stop or to reduce the dose of the offending drug. The most common AEs were gastrointestinal disorders ($n=51/111$; 45.9%) with a median time of onset at 1 month, ototoxicity ($n=22/111$; 19.8%), hyperglycaemia ($n=8/111$; 7.2%) arthralgia (5.4%) and hepatotoxicity (5.4%). We recorded 3 cases of optic neuritis from ethambutol and 2 of reversible skin pigmentation from clofazimine. The remaining 13 AEs were minor. Among the 9 patients who had 10 major AEs, 6 had severe hearing loss requiring a reduced dose of kanamycin in 4 cases and the switch to capreomycin in 2 cases. Ethambutol was withdrawn in 3 patients who developed reversible optic neuritis: they had previously taken several treatments with this drug (median: 24 months). Gatifloxacin was switched to levofloxacin in one case with hyperglycaemia and the others were controlled with oral anti-diabetics. Hyperglycaemia was reversible at the end of the treatment. We recorded no fatal events secondary to

AEs. Cure was obtained in 108 (88.5%; 95%CI 82.8-94.2) cases.

Conclusion: AEs were common in MDR-TB cases treated with short regimens. They were rarely severe, appeared early and could be easily managed without stopping more than one drug.

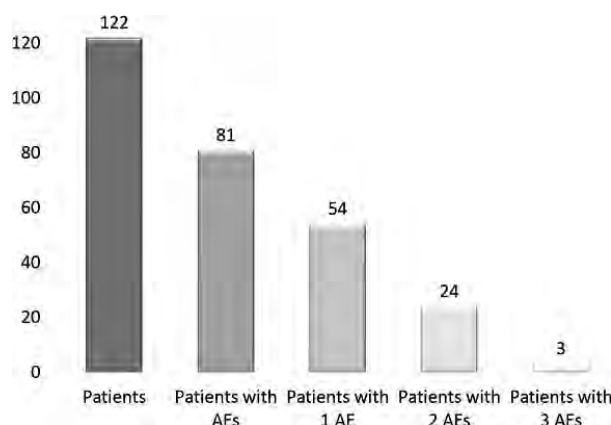


Figure Number of adverse events among MDR-TB patients.

EP-194-29 Adverse events among patients treated for multidrug-resistant tuberculosis in the Philippines

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Background: Adverse events (AEs) are important clinical considerations and often why patients are lost to follow-up (LTFU) during treatment for multidrug-resistant tuberculosis (MDR-TB).

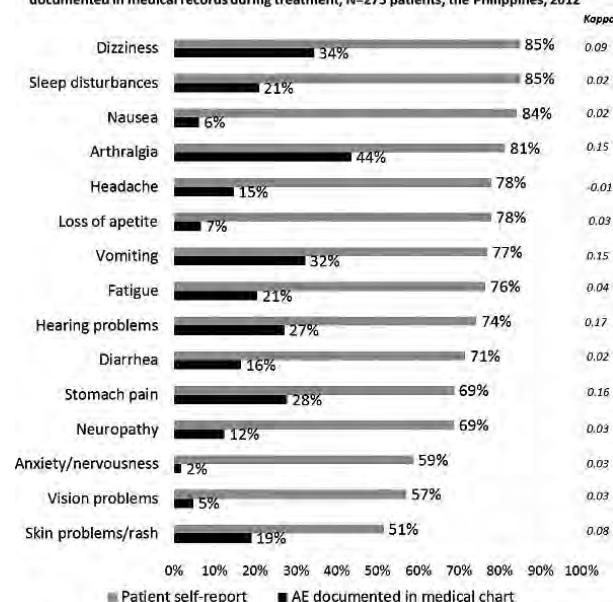
Methods: We analyzed data collected in a case-control study of risk factors for LTFU among adult patients who started treatment July 1-December 31, 2012 in the Philippines. Cases ($n=91$) were patients LTFU from MDR-TB treatment. Controls ($n=182$) were patients who were continuing treatment (for ≥ 15 months) or had an outcome of cured, completed, or failed. We collected data on AEs from medical records during treatment and in-depth patient interviews after treatment outcome, or during treatment. We used Common Terminology Criteria for Adverse Events (version 4.0) for classification of AEs. Simple kappa coefficients were calculated to measure agreement between patient self-report during interviews

and medical chart documentation of selected AEs signs/symptoms.

Results: The median time on MDR-TB treatment for case patients was 7 months; for control patients, 20 months. A total of 2,380 unique AE episodes were documented in medical records, 372 (15.6%) AEs caused regimen change, and ancillary drugs were used for 1,266 (53.2%) AE episodes. At least one AE episode was documented in 249 (91.2%) of 273 patients, with a median of 8 (range 1-35) AEs per patient. Among all 273 patients, the frequency of AEs by system organ class were recorded as follows: musculoskeletal/connective tissue ($n=173$, 63.4%); nervous system ($n=149$, 54.6%); gastrointestinal ($n=144$, 52.8%); metabolism/nutrition ($n=124$, 45.4%); ear/labyrinth ($n=74$, 27.1%); skin/subcutaneous tissue ($n=67$, 24.5%); renal/urinary ($n=31$, 11.4%); hepatobiliary ($n=24$, 8.8%); psychiatric ($n=18$, 6.6%); eye ($n=16$, 5.9%); and other ($n=156$, 57.1%) disorders. Agreement between signs/symptoms of 15 AEs included both in MDR-TB patient interviews and medical record documentation was poor (Figure), with the highest concordance for arthralgia, vomiting, hearing problems and abdominal pain (kappa 0.15-0.17). Medical records did not document AEs seriousness, severity and causality assessments.

Conclusion: AEs were reported in the majority of patients during MDR-TB treatment, but appeared to be under-recorded in medical records. Healthcare workers should be trained in effective monitoring, diagnosis, documentation, and management of AEs. This study is subject to serious limitations, including recall and survivor biases.

Figure 1. The frequency signs and symptoms of adverse events (AEs) associated with anti-tuberculosis medicines self-reported by MDR-TB patients in interviews compared with AEs documented in medical records during treatment, N=273 patients, the Philippines, 2012



11. 'How do you do it?' Using e-health to improve TB programme outcomes

EP-195-29 TB case notification by private practitioners and use of new web-based tool for patient monitoring: an Indian case study

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Background and challenges to implementation: India has missing 1 million TB cases that do not get diagnosed or notified. Private sector predominates in health care and TB treatment in India; for more than 50% of TB patients, the first point of contact are private health establishments (PHE). With an aim to establish a comprehensive tuberculosis surveillance system, to ensure quality diagnosis and standardized treatment, Government of India in 2012 declared Tuberculosis a notifiable disease and also instituted a web enabled and case based monitoring application called Nikshay. This study explains the status of case notification by PHE and use of new web based tool in two hilly states; Himachal Pradesh (Pop; 7 million) and Uttarakhand (Pop; 10 million) in 2015.

Intervention or response: Following a gazetted notification in 2012, Health authorities in both states prepared an action plan for implementation. Sensitization workshops were conducted for practitioners at state and district level. Capacity building of data entry operators for using new tool was ensured. A functional linkage and coordination mechanism was established with medical colleges through task force mechanism and Indian Medical Association (IMA) at state and district level.

Results and lesson learnt: Sensitization workshops and involvement of IMA encouraged PP to get their establishments registered and initiate TB case notification in both states. By 4Q2015 end, total 108 PHE in Uttarakhand and 553 in Himachal Pradesh have been registered in Nikshay. Similarly, total 1848 TB cases in HP and 2572 TB cases have been notified in Uttarakhand in this period. This web based application is user friendly, provides a quicker access to accurate and real time information to the program managers and PP.

Conclusions and key recommendations: Health facilities registration and TB case notification rate by PHE is steadily increasing, new web based tool is providing an accurate and real time exchange of information between PHE and health department, which is critical for instituting a support system for adherence, follow-up, default retrieval and contact tracing. However, there should be sustained efforts to sensitize each practitioner about their public health responsibility and encourage them to bring every TB patient on records.

EP-196-29 South Africa's implementation of an integrated monitoring system to manage data for TB and HIV: lessons from the pilot

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South Africa has high co-infection of TB and HIV but programme data were vertically managed. HIV and TB services are offered at over 3,700 health facilities nationally. HIV data is predominantly managed through an electronic system at facility-level whilst TB data is recorded in a paper register and digitized at a subnational level. A 2013 WHO-led evaluation, and a subsequent independent evaluation, recommended the integration of information systems. In January 2015 South Africa took the decision to integrate TB and HIV data management at the facility-level into a single non-networked electronic system. Implementation planning commenced thereafter. Establishment of a national-level technical working group (TWG) guided planning and development of technical tools, identified eleven pilot facilities, and nominated implementers. Implementers piloted the integration and change management processes. Training included clinical mentorship, clinical recording in the stationery, integrated TB and HIV data capture, reorientation of the data flow, and demonstrated use of patient management reports. Supplemental processes included strengthening district support and mentorship structures. Implementers provided feedback on lessons learnt and experiences through a standard report template. The 12-month pilot facilitated measured learning. They have informed planning including modification to the tools and software, development of the standard operating procedures (SOPs) and implementation plan, and alignment of the health management information system (HMIS). Early lessons indicate this approach has fostered understanding, assisted facilities to adapt to the changes, and enabled the sub-national levels to adapt to the new context. This has stimulated a groundswell of enthusiasm to roll-out further. The national scale-up strategy commenced in March, 2016. Implementation targets will balance the twin needs of scale-up with data quality. The implementation guide will support the required change management at the facility-level as well as higher levels. Parallel information systems fragment resources and data management. This is especially significant in the massive, generalized, co-morbid epidemics in South Africa. Integrated TB and HIV

facility systems support integrated patient management and retention and also rationalize support and management requirements. Inclusive and measured change management processes support understanding through the transition, fostering ownership and institutionalisation and lead to sustainability and support to patient management.

EP-197-29 Brazil's ten year experience in scaling up an electronic system to confront MDR-TB: lessons learned and strategies for quality improvement

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Background and challenges to implementation: A decade ago, Brazil was challenged with a lack of readily accessible data to confront the growing burden of MDR-TB cases and scale up services in a continental size country. Despite limited computer/internet infrastructure in 2005, Brazil made a bold decision to switch from paper-based to a web-based reporting system (SITE-TB) during MDR-TB program expansion. A retrospective synthesis of this experience was never done.

Response: Key informant interviews with 12 selected officials/staff representing varying levels of the health system were conducted to map their experience of using SITE-TB. An 18-item anonymous survey of all users seeking their experience based on a rating scale is ongoing. Data on amount and frequency of user's transactions and key variables of SITE-TB were investigated to determine the level of use.

Results and lessons learnt: By the end of 2015, SITE-TB was expanded to all 27 states and 295 TB units. SITE-TB facilitated a 115% increase in user transactions and 240% increase in medicines transfer among 27 states compared to 2012. Interim findings from the ongoing survey suggest that 66% of users ($n=110$) believe they have the required capacity to use all features of SITE-TB linked to their responsibilities, but were divided in their perception on the need for more training. This was validated from interviews, where state level officials believed that capacity of users must transition from routine data entry to comprehensive analysis for facility-level decision making. All key informants reported that SITE-TB promotes patient-centered management, automatically tracks adherence and assures evidenced based care with the appropriate treatment regimens. There is need for interoperability of SITE-TB with other electronic systems in Brazil particularly with patient ID for ease of tracking.

Conclusions and key recommendations: With SITE-

TB's nationwide coverage, the focus must now be on program quality improvement. A key lesson relevant for other countries is that strong leadership, assuring data quality, supportive supervision, information technology support and resources are needed to match the aspirations of scaling up digital health systems to confront the burden of MDR-TB aligned with the END TB strategy.

EP-198-29 Hospitalizations and rehospitalizations due to tuberculosis and their economic burden for the health system in an endemic city in Brazil

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Background: Hospitalizations and rehospitalizations due to tuberculosis (TB) represent an important indicator of the health weakness services for the early diagnosis and control of the disease. In Brazil, they have an expressive financial impact (frequently surpass outpatient treatment by up to 100 times), which can be potentially avoided and/or health systems could not always bear. The objective was to characterize the spatial distribution of hospitalization and rehospitalization cases by TB and the costs for the health systems in Natal, Rio Grande do Norte, Brazil.

Methods: Ecological study developed in a priority city for TB control in the country, with an incidence rate of 42.90/100 000 inhabitants. The population comprises all cases of hospitalization by TB between 2008 and 2013 obtained from the Hospital Information System of the Unified Health System. The neighborhoods were adopted as the geographical unit. The gross rates were estimated, smoothed by the Local Empirical Bayesian Method. The proportion of rehospitalization were obtained. Choropleth maps were constructed in ArcGIS 10.1. The position and dispersion measures were used to analyze the costs and an exchange rate of US\$1=R\$3.71 was adopted.

Results: In total, 569 cases of hospitalizations were identified, 102 (17.9%) of which were rehospitalizations. The spatial distribution of the events was heterogeneous and not random, being identified neighborhoods of high rates in the East and West Health Districts (Figure 1). The proportion of rehospitalization among hospitalization cases by TB ranged between 0 and 100% (Figure 2). In total, US\$ 470,370.07 was spent on hospitalization and rehospitalization by TB, with an annual mean cost of US\$ 78,395.01 and median amounts of US\$ 392.70 per hospitalization and US\$ 1,342.19 per rehospitalization.

Conclusions: The costs were considerable, especially for the health system of a region with limited

resources. The recognition of more vulnerable areas for hospitalizations and rehospitalizations by TB has promoted additional studies to understand these clusters and could support public management, moreover, developing and adopting local strategies to facilitate the access to health services can contribute to a more equitable and efficient use of the resources and the reduction of the economic and social impact of these events.

EP-199-29 Using the Management Organizational Sustainability Tool (MOST) to strengthen management systems at the National TB and Leprosy Programme in Uganda

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Background: The National TB & Leprosy Programme (NTLP) in 2013 faced several challenges that affected the potential for achieving effective control of Tuberculosis and Leprosy. Key challenges included human resources shortages; regional supervisory structures not aligned to Ministry of Health regions; limited dissemination of the NTLP mission, core values, plans and results; frequent stock out of supplies; and inadequate funding.

Intervention: Using the Management & Organizational Sustainability Tool (MOST) developed by Management Sciences for Health (MSH), the NTLP leadership mobilised key stakeholders and conducted an assessment of the various management components, prioritised a list of action areas and feasible changes, set targets, allocated roles, and identified a change leader to lead and monitor implementation. The NTLP prioritized improving the following management components: strategic and operational planning, supervision, monitoring and evaluation, community participation, human resources, and supply management. Action plans were developed and reviewed collectively on a quarterly basis to reinforce implementation and to update the list of priorities.

Results: Improvement targets were achieved for four out of six priority areas including strategic and operational planning, monitoring and evaluation, supervision, and supply chain management between 2013 and 2015 (Figures 1&2). The areas that did not improve including community participation/ACSM and Human resource management were influenced by

factors such as financing or human resource recruitment policies, which are beyond the control of NTLP. **Conclusions and key recommendations:** The MOST tool is an effective mechanism for sustainable improvement and development of management systems, especially in resource constrained settings. However, the tool may not be effective in improving elements that are significantly determined by factors external to the system being improved.

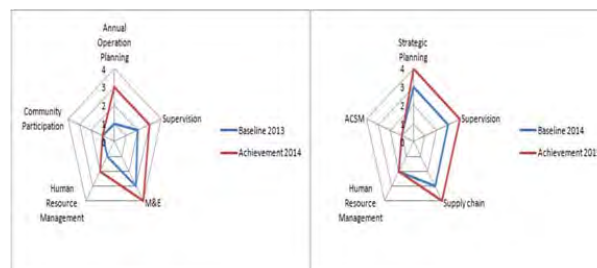


Figure Results of implementation of MOST for TB, 2013–2014 and 2014–2015

EP-200-29 Harnessing digital application to improve recording and reporting for TB control in Bangladesh: roll-out experience and opportunities

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Background and challenges to implementation: For the National Tuberculosis Control Program (NTP) of Bangladesh, accurate recording and up-to-date reporting of tuberculosis (TB) case data is a major challenge. The central manual data repository has limited variables which hinder epidemiological analysis, and lack of reliable data weakens surveillance and performance, ultimately increasing the number of drug-resistant and multi-drug-resistant (MDR)-TB patients (proportion of TB cases with MDR-TB: new 1.4% and retreatment 29%).

Intervention or response: In 2011, SIAPS assessed NTP's information management system. After an options analysis, NTP adopted the web-based e-TB Manager (e-TBM-[<http://etbmanagerbd.org/>]) to manage TB patients and generate key reports and indicators. NTP gradually rolled out e-TBM to 255 sites including all MDR sites in Bangladesh; SIAPS trained 950 staff from NTP and TB partners and developed 13 master trainers to ensure smooth functioning of e-TBM. In August 2015, NTP notified district authorities that use of e-TBM was mandatory for recording and reporting (TB10, TB11, and TB12)

TB cases; 20 districts (with full coverage of e-TBM in all sub-districts) were identified as sentinel sites where the surveillance calendar was introduced to monitor and improve data quality.

Results and lessons learnt: Pre-post analysis of 20 districts' site performance showed that 45,103 cases were entered into e-TBM against 50,836 registered cases on TB cards by December 2015. From the first to the fourth quarters of 2015, the difference in the number of registered cases between paper-based and electronically-generated reports decreased from 21.7% to 8.3%, and performance rate data (timeliness, completeness, accuracy) improved by 26.8 percentage points. NTP staff reported that e-TBM enabled them to prepare timely reports, easily analyze cases, and present at the quarterly coordination meetings to strengthen the disease surveillance system.

Conclusions and key recommendations: Use of e-TBM, along with its sustainability, has the potential to systematically organize critical surveillance data and information needed for timely decision making. With decentralization and high visibility of TB patient data, stakeholders across the health system can make real-time decisions.

EP-201-29 Investigation of tuberculosis deaths in the area of influence of COMPERJ (Petrochemical Complex of the State of Rio de Janeiro)

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Introduction: Although tuberculosis (TB) is a disease with effective treatment, diagnosis and known prevention, TB deaths continue to occur in Fluminense east, deployment area of the Petrochemical Complex of the State of Rio de Janeiro (COMPERJ). Poverty, health conditions and misconduct in the health system are likely reasons for the high number of cases and therefore deaths.

Objective: Describe the sociodemographic characteristics of deaths related to tuberculosis, and estimate tuberculosis (TB) mortality rate and whether there has been underreporting of deaths by TB in the catchment area of COMPERJ, between 2007 and 2013.

Material and methods: A descriptive study was conducted based on secondary notification data. The study population consisted of all records of the Information System deaths (SIM) which had as underlying or associated cause tuberculosis (A15.0 codes to A19.0 and B90.9 of the International Classification of Diseases and Problems Related Health - ICD 10), between 2007 and 2013, and the

cases reported in the Notifiable Diseases Information System (SINAN) as TB in the period between 2005 and 2013.

Results: During the process and analysis of the SIM database, we identify 525 deaths related as tuberculosis, and 75.6 % were male; 77.0% adults (would be between 40 years and older); 64,6% black people; 57,1% were single and 29,3% had less than three years of education. Of TB-related deaths, 392 (74,7%) lived in São Gonçalo area ; the average death rate from TB, between 2007 and 2013 period was higher than state and national averages, ranging from 5,15 to 3,69 deaths. Of the 525 TB-related deaths recorded in SIM, 65,3% were found not notified in SINAN, representing an increase of 4,9% if they were included in the notifications during the period.

Conclusions: This study highlighted the importance of using the SIM database as a strategy for improving tuberculosis information quality and identifies cases that go unnoticed by the health services.

EP-202-29 E-Office as an effective tool for E-Governance in the TB control programme, Delhi, India

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Background: Role of E-governance as an instrument in speeding up reforms is an acknowledged fact. Information and Communication Technology (ICT) tools help to improve governance, increase effectiveness, transparency and accountability. E-Office is an ICT enabled workflow based system having features of manual handling of files in an E-File mode. The study aims to assess the efficacy of E-Office system in Delhi by examining the association between various dimensions of E-Governance and TB program outcomes, before and after E-Office transition.

Intervention: Revised National Tuberculosis Control Program Delhi transitioned to E-Office system in September 2015. All files processed on E-Office from September 2015-February 2016 were examined. E-Office dimensions like E-Office Preparedness, Efficacy, Accountability and Transparency were studied on predesigned semi- structured questionnaire. Efficacy was studied in relation to Time to fund flow for variables like Salary, Training, Procurement, Monitoring, Evaluation, and calculated as time taken for the activity. TB Program outcome parameters were studied from secondary program data. They were i) Total TB case detection rates ii) Human Resource

trained iii) Smear Conversion rates iv) Infrastructure for rapid molecular labs for Drug resistant TB (DRTB) v) DRTB Case detection rates, were assessed in relation to Time to fund flow. As DRTB case management poses greater challenge, univariate linear regression was deployed on SPSS version 16 to understand the dynamics associated with DRTB case detection, before and after E-Office transition.

Result: Decreased Time to fund flow (7 days in physical form of file movement to 48hrs in E-Office) was associated with improved TB program outcomes in the State. In the study period, Total TB Case detection improved by 3% (282/100 000 population vs 273/100 000 population in previous year), 16% increase in trainings undertaken, 4% improvement in smear conversion rates for new TB cases, two times increase in infrastructure for rapid molecular labs and 8% increase in DRTB case detection, as compared to same period previous year. E-Office was found to be a significant variable for DRTB case detection ($P < 0.05$) in the State.

Conclusion: E-Office fast tracks fund flow processes, improves program accountability and impresses as an effective tool for E-Governance in high TB burden settings.

EP-203-29 Health network patient navigation and bridge case management: migration need never be an impediment to effective TB treatment

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Background and challenges to implementation: An estimated 244 million people were classified as international migrants in 2015, a population that would comprise the world's fifth largest nation. Mobility is a defining characteristic of modern society, creating unpredictable patterns of disease and challenges to the delivery of medical care. Few health care systems are structured to address the unique health problems posed by highly mobile populations. Losing track of patients often leads to increased costs as previously conducted screening and treatment are repeated and reestablished with the potential of leading to resistant disease. Health systems are unable to report the outcomes on patients whose care they have initiated yet financially are unable to commit the considerable resources that a site specific patient navigation system would require. **Intervention or response:** MCN created Health Network (formerly TBNNet) to address the unique challenge of mobility by creating a system that ensures patients can have appropriate continuity of care. Health Network provides critical patient navigation, bridge case management, medical records

transfer, resource identification and evaluation, referral, and education for migrant patients requiring care for tuberculosis as well as surveillance support to various NTPs.

Results and lessons learnt: Between 2005 and 2014, Health Network provided services to 1,641 culture confirmed cases of TB disease traveling from the USA to 81 different countries of the world. Of these, 1,378 cases have confirmed treatment outcomes for a completion rate of 84%.

Conclusions and key recommendations: Migration need never be an impediment to completion of treatment for TB disease or infection. Health Network provides a model of international public-private collaboration that aims to ensure TB treatment completion among mobile populations. The key elements of the program include record transfer, patient navigation, and personalized case management. These elements create a network of support that facilitates effective treatment leading to decreases in disease among some of the most vulnerable patient populations. Utilization of Health Network could also assist with the standardization of TB treatment globally.

12. Got the bug? Basic science

EP-204-29 Induction of TB protection and lung-resident memory in mice by a Sendai virus-based vaccine

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Background: Hitherto failures to generate better protection by novel TB vaccines may be related to failures to adequately establish specific resident immunity in the lung. Respiratory virus vectors target the lung and raise immune memory there. We tested if this would be an effective approach for TB with a novel vaccine and assessed the role of CD8 T cells.

Methods: A crippled Sendai virus vector was used as an intranasal vaccine to express antigen 85AB in mice. It was administered either alone or two months after vaccination sub-cutaneously with BCG. Effects on lung, lymph node and spleen T cell immunity and pathology were measured, in addition to impact on TB challenge infection. The involvement of CD8 T cells was assessed by administering a CD8 T-cell-neutralizing antibody in vivo.

Results: When given alone the vaccine induced

substantial numbers of lung-resident memory CD8 T cells whereas BCG did not and protective effects were similar. In contrast, when given as a boost to BCG greater protection from challenge infection was obtained and this was associated with lung cells being primed for a much greater specific CD8 T cell response.

Conclusions: Inadequate induction of CD8 T cell immune memory in the lung may underlie the failure of TB vaccines. Boosting with a mucosal vaccine such as SeV85AB offers a superior approach.

EP-205-29 Long-term survival studies of a novel, live-attenuated tuberculosis vaccine in the guinea pig model

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Background: *Mycobacterium tuberculosis*, the causative agent of human tuberculosis (TB), claims over a million lives annually despite wide use of the historic Bacillus Calmette-Guerin (BCG) vaccine. The variable efficacy (0-80%) of BCG against pulmonary TB in post-adolescents underscores the urgent need for a more efficacious TB vaccine. To this end, we have developed a novel intranasal (i.n.) vaccine, PathVac85B, based on a naturally temperature-sensitive, aquatic *Mycobacterium* species expressing *M. tuberculosis* antigen 85B.

Methods: Our previous results showed that vaccination with two doses of i.n. PathVac85B lowers lung bacillary load and reduces lung lesions six weeks post *M. tuberculosis* infection in vaccinated guinea pigs. In the present study, we compared the long-term efficacy of two-dose i.n. PathVac85B administered 3 weeks apart to intradermal (i.d.) BCG vaccination and unimmunized guinea pigs. Following immunization, the animals were rested for 10 weeks before skin testing and low-dose aerosol challenge with *M. tuberculosis* strain Erdman. Six weeks post-infection, 5 animals from each group were euthanized and examined.

Results: 45% of the PathVac85B-vaccinated animals and 100% of the BCG-vaccinated group developed a positive tuberculin skin test result, while all of the unvaccinated animals were negative. Gross lung pathology showed that all animals in the PathVac85B and BCG groups exhibited reduced numbers of and smaller granulomas than in the unimmunized animals. Lung histology of the unimmunized animals revealed larger areas of consolidation with central necrosis than those vaccinated with either PathVac85B or BCG. The lung bacterial loads were lower in both vaccinated groups compared to the unvaccinated controls. The remaining fifteen animals per group were observed for an additional 24

weeks. Ten of 15 unvaccinated, 12 of 15 PathVac85B-vaccinated, and 12 of 15 BCG-vaccinated animals survived the duration of the study. Lung histology revealed that the vaccinated animals had statistically lower percentages of total affected lung area, tissue mineralization, and primary lesions compared to unvaccinated animals.

Conclusions: These results indicate that protection conferred by two-dose i.n. PathVac85B is comparable to i.d. BCG. Future studies will include examination of protective efficacy of PathVac85B and next-generation derivatives expressing additional protective antigens using a more-virulent challenge strain.

EP-206-29 Opsonic monoclonal antibodies directed against *Mycobacterium tuberculosis* enhance blood clearance in a quantitative qPCR mouse model

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Introduction: Impaired immunity allows rapid progression of tuberculosis (TB), and in HIV patients may result in highly lethal *Mycobacterium tuberculosis* sepsis. Rapid diagnosis of *M. tuberculosis* bacteremia and immune enhancing therapies may improve treatment of *M. tuberculosis* sepsis and enhance therapy of MDR and XDR-TB.

Objective: To identify and characterize monoclonal antibodies (MABs) directed against *M. tuberculosis* that promote opsonization and killing of mycobacteria and enhance *M. tuberculosis* clearance from the blood.

Methods: Mouse monoclonal antibodies (MABs) directed against *M. tuberculosis* were produced by immunizing mice with ethanol killed *M. tuberculosis* (EtOH K-MTB) and screened by ELISA for binding to several *M. tuberculosis* strains (Erdman, HN878, and CDC1551). Additionally, these MABs were analyzed for *M. tuberculosis* opsonic activity by microscopy and mycobacterial opsonophagocytic killing activity (OPKA) using *M. smegmatis* and HL60 or U937 cells. MABs with OPKA >50% were subsequently evaluated in a mouse *M. tuberculosis* blood clearance model using killed *M. tuberculosis* TB strains and *M. tuberculosis* qPCR.

Results: MABs that bound to killed *M. tuberculosis* strains in the ELISA assay also enhanced OPKA in both HL60 and U937 cells (>50% killing over baseline). In addition, MABs that exhibited OPKA also enhanced clearance of Killed MTB within 24 hours of challenge. Mice challenged with HN878 bacilli that were given MAB GG9, cleared the *M. tuberculosis* from the blood by 24 hours (qPCR

$C_T=40$ for both 6110 and 1081 targets); 7/10 (70%) mice given 5, or 10 mg/kg of anti-*M. tuberculosis* MAB GG9 cleared the bacteria from the blood compared to 1/5 (20%) PBS treated control mice.

Discussion: Using qPCR to detect *M. tuberculosis* in the blood of mice challenged with killed *M. tuberculosis* strains is an efficient methodology to identify MABs that may promote mycobacterial phagocytosis and enhance clearance of *M. tuberculosis* from the blood. Since *M. tuberculosis* sepsis is rapidly fatal, anti-MTB MABs that enhance clearance of *M. tuberculosis* from the blood might improve the effectiveness of antimicrobial therapy for *M. tuberculosis* sepsis. In addition, MABs may provide adjunctive therapy for patients with MDR or XDR-TB.

EP-207-29 HIV but not active tuberculosis increases CD4 expression in monocytes in peripheral blood from Senegalese patients

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Background: Previous studies have shown an increase in the number of monocytes during the active phase of tuberculosis (TB), and the activation of those monocytes, associated with an increased expression of the CD4 receptor. The objective of this work was to evaluate the monocytic profile in HIV and tuberculosis co-infected patients.

Methods: We recruited 195 subjects in Dakar, Senegal, of whom 95 had no clinical TB (37 were HIV- and 58 HIV+), and 100 patients were diagnosed with confirmed or probable TB (17 HIV- and 83 HIV+). Each sample was analyzed with Trucount-based panleucocytometry on a FACSCalibur flow cytometer. Absolute counts and Mean Fluorescence Intensity (MFI) were determined for monocytes in each of the 4 groups (TB+HIV+, TB+HIV-, TB-HIV+ and TB-HIV-) and compared with Kruskal-Wallis.

Results: Monocyte counts did not show any significant difference between the 4 groups ($P = 0.350$). However, MFI values were significantly different ($P = 0.0012$), with a higher value for HIV mono-infected patients (MFI 229 UI) compared to co-infected patients (MFI 201, $P = 0.0221$) and to TB mono-infected patients (170, $P = 0.0013$).

Conclusions: We did not observe any change in monocyte counts or CD4 expression due to TB. On the contrary, HIV was associated with an increase in CD4 expression

EP-208-29 The potential for dextrans to modulate the immune response of mycobacteria-infected macrophages

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Background: Dextran is a polysaccharide used for intravenous infusions from 1940th, while oligodextran (or isomaltooligosaccharide) has been used as a food supplement from 2000th. Dextran is reported to exacerbate experimental tuberculosis in guinea pigs, while its derivative, oxidized dextran, suppresses BCG-induced granuloma formation and fibrosis in mice. Dextran binds mannose receptor of macrophages and therefore could modulate the immune response of these cells that play key roles in granuloma formation. We studied how dextrans change the cytokine response of human macrophages to mycobacteria.

Methods: Human monocyte-derived macrophage were pre-treated with dextran 66 (average MW = 66 kDa, D66) or oligodextran (20.6 kDa, D06) 30 minutes before infecting with *M. tuberculosis* (H37Rv) or *M. bovis* (BCG, 2.5×10^6 CFU). IFN- γ and IL-10 concentration in the media were analyzed using ELISA, while IFN- γ , IL-10 and TGF- β 1 mRNA levels were measured in cells using qRT-PCR at days 1 and 7 post-infection (p.i.). For immunoassay data, the IFN- γ /IL-10 ratios were ranked as anti-inflammatory (0-0.3), not biased (0.3-2.0) and pro-Th1 (2.0 and higher).

Results: The results indicate that on day 7 p.i., the IFN- γ /IL-10 ratio in H37Rv- and BCG-infected groups pre-treated with dextran were 2.5 and 3.4 times higher, respectively, compared to infected only controls, while oligodextran pre-treatment resulted in a 1.6 and 16.8 times increase, respectively, compared to infected controls. Moreover, dextran and oligodextran decreased the relative levels of TGF- β 1 mRNA in H37Rv-infected cells 1051 and 57 times, respectively, on day 7 p.i., while changes in IFN- γ and IL-10 mRNA levels were no different.

Conclusions: Dextrans are safe and inexpensive compounds that bind the mannose receptors on macrophages and probably interfere with the mannose receptor-dependent signaling activated by mycobacteria. We have shown that dextrans can influence regulation of extracellular matrix remodeling by human macrophages by decreasing TGF- β 1 expression and to promote pro-Th1 responses by increasing IFN- γ /IL-10 ratio.

EP-210-29 A translational modelling and simulations approach to exploit pre-clinical tuberculosis data

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Background: Development of novel therapeutic drugs and therapeutic regimens in tuberculosis research is time-consuming and resource-intensive. In order to exploit pre-clinical *in vitro* information on tuberculosis drugs utmost, the present study aimed at defining and evaluating a translational approach using the recently developed Multistate Tuberculosis Pharmacometric model (MTP model, Clewe et al. JAC 2015) for prediction across *in vitro* systems, to animals and to humans, using rifampicin (RIF) as model drug.

Methods: For translational prediction, estimates from a static *in vitro* system combining both log- and stationary phase RIF effects were used as origin system for translation. The MTP model was extended to capture (i) persistent drug effects originating from post-antibiotic effect studies, (ii) differences in mycobacterial susceptibility by a MIC-based scaling approach considering MIC uncertainty and/or MIC distribution (e.g. from EUCAST), (iii) growth properties of mycobacteria in the target system (i.e. log- or stationary phase, carrying capacity), (iv) protein binding and plasma/target site exposure (if applicable). The extended MTP model was used to predict *in vitro* hollow-fiber, a murine dose fractionation study for determination of PK-PD indices and a 14 day clinical trial of RIF 10 mg/kg daily to determine early bactericidal activity (EBA). 'R'-software (version 3.2.1) was used for simulation and data processing.

Results: The extended MTP model successfully predicted hollow-fiber experiments for RIF. The result of a murine PK-PD study was also well predicted and the PK-PD indices AUC/MIC and C_{max}/MIC were correctly identified. Using clinical trial simulations, the PK-MTP model predicted mean $EBA_{0-2days}$ of 0.160 log CFU/mL/day [90% prediction interval (PI_{90}): 0.074-0.364] and mean $EBA_{0-14days}$ to 0.143 log CFU/mL/day [PI_{90} : 0.055-0.251], which was well in agreement with the observed clinical result for RIF from several clinical trials.

Conclusion: The MTP model was successfully applied for translational prediction from *in vitro* time-kill experiments to hollow-fiber, animal and clinical studies for determination of EBA. The present study sets the basis for further systematic evaluation of translational predictions with further tuberculosis drugs and drug combinations.

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EP-211-29 BCG vaccination in sub-Saharan Africa: coverage, geographical variations and the hotspots

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Background: Tuberculosis (TB) remained a foremost cause of morbidity and mortality in children and adults. TB affects and kills more adults aged between 15 and 59 years than any other infectious disease globally. About 15% of TB patients are co-infected with HIV infection with as many as 50-80% of these patients living in sub-Saharan Africa. Over the decades, Bacille Calmette-Guerin (BCG) vaccine has been part of Expanded Programme on Immunisation in many African countries and documented to provide protection against TB meningitis and disseminated TB in children. This study seeks to evaluate the level of coverage for BCG vaccinations, geographical variation and to identify the 'hotspot of low performance' among sub-Saharan Africa countries with respect to TB Control Programmes.

Methods: The study used data from the cross-sectional, population-based Demographic and Health Survey (DHS) from different countries in sub-Saharan Africa. The study involved 29 countries with DHS that are within the time frame of 2010-2015. Descriptive and spatial data analysis methods were used to determine the coverage level and geographic variation in children aged 12-23 months who received BCG vaccinations at any time before the survey. Kruskal-Wallis test was also used in the analysis.

Results: The BCG vaccination coverage ranged from 51.2% in Nigeria to 99.1% in Rwanda. On average, the countries of West African, Central/East African and Southern African sub-regions recorded 88.1%, 90.1% and 92.9% respectively. There was no significant differences among the three African sub-regions, $P=0.887$. Various regions of Burkina Faso, Burundi, Ghana, Kenya, Liberia, and Tanzania had 100% BCG vaccination. However, Nigerian North East and North West regions, Ethiopian Affar and Somalia regions had the lowest performance at 21.7%, 35.1%, 38.1% and 45.7% respectively.

Conclusions: The use of both statistical and geographic system analysis contributes to better understanding of the geographical disparity and identification of poor performing areas for BCG vaccination coverage among children in sub-Saharan Africa. This is useful for customising intervention strategies for local regions, countries and more efficient allocation of limited resources. This is vital for various TB control programmes in sub-Saharan African countries.

EP-212-29 Adverse events monitoring for two types of BCG vaccination in Russia

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Background: Wide BCG vaccination coverage (which is carried out later than 3 days after birth) in Russia (97%, 2014) requires the organization of monitoring of adverse events of vaccination (AE) which has been realized based on computerized register since 2000.. Special interest was to evaluate AE for two type of BCG vaccine used in the country: standard vaccine dose - 0.05 mg ('BCG1') and vaccine with a twice reduced content of the weight of Mycobacterium BCG vaccination dose - 0.025 mg ('BCG-M'). BCG-M use for primary immunization and vaccination for newborns in the regions of Russia, where the TB incidence rate is less than 80 per 100K and for HIV-contacted newborns.

Methods: Analysis of data of 3769 children with AE of vaccination, including 2725 after BCG vaccination and 1044 after BCG-M, from 49 Russian regions, registered in 2000 –2013.

Results: The clinical structure of AE after BCG vaccination included: local abscess (LAb) in 775 (28%; 95%CI 26.8-30.1); lymphadenitis (LPh) in 1566 (57.5%; 95%CI 55.6-59.3), osteitis (OSt) in 372 (13.7%; 95%CI 12.4-14.9), disseminated BCG (DBCG) in 12 (0.4%; 95%CI 0.2-0.7) children. The clinical structure of AE after BCG-M vaccination included: LAb in 466 (44.6%; 95%CI 41.6-47.7), LPh in 422 (40.4%; 95%CI 37.4-43.4) OSt in 140 (13.4%; 95%CI 11.3-15.5), DBCG in 16 (1.5%; 95%CI 0.8-2.3) children. All types of AE for BCG-M were less common ($P < 0.01$) than for BCG, except OSt ($P > 0.05$).

Conclusions: AE monitoring gives opportunities to investigate the AE structure in order to determine their possible connection with vaccine quality, a violation of the rules of its transportation, storage and use. BCG-M provides a lower level of AE.

EP-213-29 Epidemiology of BCG disease in Iraq, 2010-2015

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Background: BCG vaccine is considered to be safe and has a low incidence of serious adverse events. The most common complications after receiving BCG are local reactions and regional lymphadenopathy.

Methods: This is a cross-sectional record based study that collected data by reviewing the electronic registers of national tuberculosis program (Electronic

Nominal Recording System) for all Iraq for the years 2010-2014. Targeted patients were patients presented in their first two years of life with Extra pulmonary TB disease (axillary/cervical lymphadenopathy or cutaneous manifestations) and were recorded as TB disease complicating BCG immunization.

Statistical analysis: Crude analysis was done using cross tabulation and simple plotting.

Results: The review of records found that out of 45615 patients recorded in Iraq during 2010-2014, 279 patients were recorded as BCG disease at a rate of 0.6% (6/1000) out of all TB cases, around 26% out of all under five (U5) TB cases and 41% out of all Extrapulmonary U5 patients. Maximum notification of BCG disease was during the year 2011 when 84 cases notified at a rate of 0.9% out of all TB cases and around half Extra pulmonary U5 cases. Males constituted 185 cases (66.3%) and remaining 94 were females (33.7%). Clinically, 246 patients (88.2%) presented as local or regional lymphadenopathy (163 male and 83 female) and 33 patients presented as suppurative skin lesion at BCG injection site (22 male and 11 female). There was not significant association between the presentation form and patient sex ($P=0.963$). Geographically, the highest contribution to recorded patents was from Baghdad and least from Muthanna. This distribution was consistent with population distribution in these governorates. Final diagnosis relied upon microscopical finding of acid fast bacilli in 7% of cases, on histopathological reports in 48%, and on clinical basis in 45% of cases. Treatment outcome was generally benign: out of documented 200 treatment outcomes, success of treatment was observed in 188 (94%) of patients, 8 (4%) were lost to follow up during treatment and 4 (2%) died.

Conclusions: Though BCG disease has generally a benign course, it constitutes a considerable proportion of U5 TB cases in Iraq.

13. Smoke-free environment

EP-214-29 Evidence from an integrated mass media campaign to support Beijing's 100% smoke-free law

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Background: On June 1st, 2015, the 100% Smoke Free Law came into effect in Beijing- the capital of China with 20+ million population. To support the implementation of Beijing's 100% SF law, Vital Strategies collaborated with Beijing government-

Beijing Patriotic Health Campaign Committee (BPCC) and Beijing Tobacco Control Association (BTCA) to conduct an integrated four-week mass media campaign, commencing on the effective date of the law, June 1st, which is National Children's Day in China, the campaign was designed to increase understanding of the harms of SHS exposure, particularly to children, and to support enforcement of the law by increasing awareness of the law's implementation and encouraging compliance. The campaign featured a new television PSA, *Smoke-free Restaurant*, which was tested and refined through message testing research. The ad highlights specific dangers of SHS exposure for children, incorporating video from adaptation of hard-hitting *Cigarette Are Eating Your Baby Alive originally from USA*, and emphasizes the benefits of the SF law in providing protection from these harms.

Methods: To evaluate the campaign impact, scientific-developed population door-to-door surveys were conducted in urban and peri-urban areas of Beijing from July 1st to August 12th in a total of 900 households.

Results: The evaluation showed positive results for the Beijing smoke free campaign. The survey found that 86% reported seeing or hearing information or advertising about smoking and health in the previous two-months. Almost one-third in urban and peri-urban districts of Beijing (29%) recalled seeing the campaign Smoke-free Restaurant ad, representing recall of campaign exposure by approximately 4.67 million people aged 15-55 years old. The Smoke-free Restaurant ad was found to have communicated effectively, with a strong majority of campaign-aware respondents reporting that it was easy to understand (98%), personally relevant (91%), provided new information (90%), and made them stop and think (81%). The most commonly reported messages recalled from the ad related to the harms of SHS exposure (61%), the harms of smoking (47%) and the new smoke-free law (36%).

Conclusions: Well-developed integrated mass media campaign with SHS harm message effectively supported the implementation of newly passed 100% smoke free law in Beijing, China.

EP-215-29 Environmental tobacco smoke as a risk factor for increasing childhood respiratory infection and pneumonia in South-West Region, Nigeria

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Background: There is consistent evidence that children exposed to environmental tobacco smoke (ETS) have higher incidence of asthma, ear- and throat

disease, worsening of asthma symptoms and lung symptoms as cough, wheezing and pneumonia. A child exposed to ETS has about 30% higher risk of absence from school due to illness. Evidence clearly implicates (ETS) as a cause of lung cancer, excess respiratory disease, and cardiovascular disease mortality in non-smokers. Few studies have looked at the interaction of tobacco use or ETS exposure with occupational and ambient air pollution (both indoor and outdoor) in contributing to chronic obstructive pulmonary disorders in developing countries, or the importance of ETS as a risk factor for the already high burden of childhood respiratory infections.

Method: A descriptive cross sectional study was carried out in 5 states (Ogun, Lagos, Akure, Oyo and Ekiti). A multistage cluster random sampling was employed to select 450 families in each state. Data was collected using structured questionnaires by trained interviewers.

Result: About 2115 records were available for analysis. There were 1208 (60.7%) males and 815 (38.1%) females aged 10 and below. A Majority, 807 (38.0%) live with both parents, 213 (10.0%) live with mother alone while 265 (12.5%) live with relatives. The prevalence of children exposed to ETS in the southwest region Nigeria was 73.2%, the study further revealed that 28.5% of children in this region with respiratory childhood infection are exposed to environmental tobacco smoke and 18.4% pneumonia cases are attributed to ETS. However, (122, 14.7%) parents or relatives don't see a problem with using tobacco products. It is also clearly stated that about 46.9% cases of respiratory childhood infection and pneumonia combined are caused by ETS in the south west region Nigeria.

Conclusion: Since Environmental Tobacco Smoke has this much negative effects on children in the south west region Nigeria. Efforts should be tailored towards protecting children from ETS to reduce the rate of children exposed to ETS, thereby curbing or reducing respiratory childhood infection and pneumonia in Nigeria

EP-216-29 Implementing tobacco control policy in a teaching hospital: case study of a tobacco-free medical college in Northern India

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Background and challenges to implementation: Indira Gandhi Medical College and Hospital (IGMC) Shimla in Himachal Pradesh is one of the largest and oldest teaching institutions in Northern India having near 1000 bed strengths and records more than 1500 daily OPD registration. Indian tobacco control legislation (COTPA) bans smoking in public places and sale of tobacco products in and around an

educational institution; however the implementation has been sub-optimal. The present case study enumerates the steps taken by the department of hospital administration to make IGMC- a model tobacco free educational institution.

Interventions or response: A high level institutional core committee for tobacco control was constituted. A strategic and comprehensive action plan was formulated. Department wise nodal officers were notified to ensure enforcement in respective departments and buildings. Circular was shared to all departments, students and employees association to comply with the law. Signage as specified under the law were displayed at all prominent places in campus. Several boards having anti-tobacco messages were displayed across the hospital campus, walls and also on OPD slip. Strict law enforcement was ensured, till date more than 400 violators has been punished and fine amount of Rs 76630/- has been collected.

Results and lesson learnt: There is an overwhelmingly positive response from all sections of peoples, employees, students, patients and visitors. The smoking has been literally banned throughout the campus. Department of hospital administration is doing regular monitoring of enforcement activities. The number of people seeking tobacco cessation services in the TCC is increased; from January 1, 2014 till date 350 persons has sought help from TCC to quit tobacco. There is no tobacco selling shop inside and within 100 yards of the premise. The institute qualifies for the model tobacco free educational institution.

Conclusions and key recommendations: IGMC and associated hospitals becomes a model for tobacco free educational institution in India demonstrating successful implementation of tobacco control policies. Other tertiary care health institutions and teaching hospitals in India or in similar settings in other countries can also be made tobacco free educational institutions. Tobacco-free campuses are a great public health initiative.

EP-217-29 Government, NGO and army defeat all obstacles through innovations in achieving high compliance with smoke-free provisions in East Siang, a difficult hilly area

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Background: Indian tobacco control legislation (Cigarette and Other Tobacco Product Act-2003) prohibits smoking in public places. The law mandates that a specific signage informs people about smoke free status of a public place must be displayed at prominent places. Under the law, violators of the

smoke free provisions will be fined up to INR 200/ East Siang ,a hilly district of Indian state of Arunachal Pradesh implemented various steps for enforcing smoke free legislation through massive awareness activities, series of capacity building programmes followed by effective law enforcement. This study conducted with an objective to assess the current level of compliance to the smoke free provisions of the law.

Methods: Smokefree compliance surveys are important tools to validate levels of compliance. An unobtrusive cross sectional survey of randomly selected 135 public places in four clusters of district was done in the month of June,2015 by trained investigators using pretested checklist. The five core parameters of evaluation were: Presence of signage, absence of active smoking, absence of smoking aids, absence of tobacco litter and absence of tobacco smell.

Results: The 'No smoking signage' informing general public and tourists about smoke free provisions were observed at 99 % of public places; While 98.2% of public places were found without active smoking. 96.21% public places were observed free from Smoking aids like ashtrays, match boxes & lighters. More than 97.4% of sampled public places didn't have any tobacco litter (cigarette butts and bidi ends). Over 98.2% of public places dint have evidence of recent smoking as evident of absence of tobacco smell.

Conclusions: East Siang district has achieved high level of compliance to smoke free provisions of the legislation as a result of increased awareness among general public and custodians of public places. Robust enforcement mechanism established. Pro-active district administration involved all important stakeholders led to this historic achievement. The administration has declared East Siang as first smoke free district of the state. This model has motivated and speeds up the Implementation mechanism of tobacco control in entire hilly and difficult state.

EP-218-29 Smoke-free homes: a step further in prevention of second-hand smoke and delaying initiation

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Background and challenges to implementation: 35% Population of the India is consuming the tobacco products out of them 14% (110.2 Millions) are Smokers according to the Global tobacco adult survey (GATS) 2009-2010. The main concept of 'Smoke free Homes' (SFH) to formulate the rule and moral ethics to protect the vulnerable peoples from the second hand smoke (SHS). According to the WHO in India 10% out of total deaths every year due to tobacco are due to the exposure of second-hand

smoke. Which is 80,000 to 1, 00,000 deaths per year. As we know due to the implementation of COTPA 2003 and Public Awareness the trend smoking in public places is declining. But still the most vulnerable place for the SHS exposure is Homes upto 50% exposure to SHS. So advocating a home smoke free we can protect the people from SHS exposure within their Homes.

Intervention or response: As a pilot project of promoting Smoke Free Homes, City Mohali from Punjab was chosen and Implementation of prohibition of Smoking in public places of Mutli Unit Homes was carried. for the same the concerned departments were sensitized to issue directions for the same.

Multi Unit homes were approached to voluntarily declare their homes as Tobacco Smoke Free and motivate others for the same. Multi Units chosen because people life in close contact with each other. During advocacy main focus was on health effect of SHS on children and impact on their minds in considering smoking acceptable.

Results and lessons learnt: Notifications from the Building and Housing Welfare Deapartment were issued making it mandatory for the existing, under construction and upcoming multi unit projects to make their premises completely free from smoking at common places within boundary.

Out of total 600 homes in two multi unit societies 375 homes voluntarily declared their homes smoke free prohibiting anyone to smoke in their house.

Conclusions and key recommendations: People ready to try the concept of Smoke free homes as it safegaurd their families. House of smokers where children were present, agreed to try to quit when sensitize about the physical and mental harm.

EP-219-29 Students' perceived effectiveness of a tobacco-free campus policy

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Background: Tobacco-free (TF) college campus policies have the potential to be a high-impact tobacco control strategy, with over 1,100 TF campuses in the U.S. The purposes were to 1) determine demographic and personal characteristics associated with students' perceived effectiveness of a TF campus policy; and 2) assess whether tobacco use status and exposure to secondhand smoke (SHS) predicted perceived effectiveness.

Design/methods: Using a non-experimental, cross-sectional design, 5,000 randomly-selected students from a southeastern university in the U.S. were invited to participate in an online survey in April 2013. With an overall participation rate of 14.8%, 660 were included in the sample for this study: 72%

female, 79% White/non-Hispanic, 14% used cigarettes, 8% used non-cigarette tobacco product (s). Two indicators of effectiveness (reduced SHS exposure and encouragement to quit) were assessed 3.5 years post-policy. Proportional odds models determined the predictors of the two policy effectiveness indicators.

Results: Approximately 60% believed the policy was very or somewhat successful at reducing SHS exposure. Males and lower undergraduate students thought the policy was less effective, compared with females and graduate students ($P = 0.006$). For each 1-point increase in self-reported exposure to SHS, policy's effectiveness in reducing SHS exposure decreased by 27%. Only 40% of participants believed the policy was successful in encouraging quitting tobacco. Males were less likely than females to indicate policy effectiveness in promoting quitting ($P = 0.040$). International students were 140% more likely to rate the policy as more effective relative to quitting, compared to domestic students ($P = 0.013$). Compared with those not using any tobacco products, cigarette users were 38% less likely to rate the TF policy effective in encouraging quitting ($P = 0.029$).

Conclusions: Six of 10 students viewed the policy as effective in reducing SHS, but only 40% thought the policy encouraged quitting. Perceived effectiveness of TF policies may be related to compliance with the policy. Targeting males, undergraduate students and tobacco users is imperative when aiming to improve compliance with TF campus policies. Objective measures of effectiveness (e.g., observations and cigarette butt collection) and tobacco use behaviors are needed to fully measure the success of TF campus policies.

EP-220-29 Substantial decrease in exposure to second-hand smoke with strict implementation of smoke free laws: the case of Punjab, India

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Background: Second hand smoke (SHS) has adverse health effects on men as well as women with grave health implications for the next generation. Section 4 of Indian Legislation, Cigarettes and Other Tobacco Products Act (COTPA) prohibits smoking in public places, thus protecting people from SHS. The state of Punjab was among the pioneers in India in strict implementation of COTPA, the measures include ban on loose cigarettes, involvement of stakeholders from different departments, issuing *challans* (monitory

finer), which led to declaration of Punjab as first large 'Tobacco Smoke Free' State of India. The present study was conducted with an objective to assess the exposure to second hand smoke at home and indoor working areas in Punjab, India.

Methods: The present cross sectional study was conducted in the period of December 2015 till March 2016. A three stage sampling technique was used for collecting data from three randomly selected districts (administrative divisions) representing three major regions of Punjab, India. A sample size of 510 individuals was divided equally into urban and rural area with proportionate sampling on basis of subsets of age groups and gender. The questionnaire based on Tobacco Questions for Survey (TQS), a subset of key questions from GATS were used during interview with respondents. Ethical consent from Institution Ethics Committee was duly obtained prior to data collection.

Results: At home, SHS exposure was higher in non smoker females (18.8%) than males (12.8%). At work place, SHS exposure was higher in non smoker males (26.4%) than females (16.2%). It was higher in urban areas than in rural areas. The SHS exposure was associated with educational background (OR-2.3, CI-1.7-3.4), low socio-economic status (OR-3.1, CI-1.9-3.9), and employed groups (OR-2.9, CI-1.7-3.2) as compared to their counterparts.

Conclusion: Accelerated implementation of comprehensive smoke-free policies in Punjab has resulted in substantial decrease in exposure to SHS when compared with data from GATS 2009-10. Policy-makers should adopt policies consistent with Article 8 of the World Health Organization Framework Convention on Tobacco Control and its guidelines and public health education to promote smoke-free households and workplaces.

EP-221-29 Compliance with local smoke-free legislation in Bali Province after 4 years implementation: a serial survey

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Background: Since 2011, the local government of Bali Province implement a local legislation no. 10/2011 regarding smoke-free area or local smoke-free legislation (LSFL). Comprehensive evidence is needed to support the successful of the implementation in the

future. We aimed to describe the compliance to the legislation and identify the factors associated.

Methods: This is a serial survey that conducted 5 times every 6 month, started at 2nd semester 2013 until 2nd semester 2015. The population is all areas that ruled in the LSFL including education facilities, health facilities, worship places, children's playground, work places and public places. The Number of samples at each study is 1100 and selected by proportional probability to size (PPS). The compliance defined by 8 criteria that established in the LSFL. The data were collected by observe the indoor and outdoor area of building using checklist and interviewing the managers.

Results: The study succeeded to observe 6670 buildings of 5500 smoke-free area selected. The compliance to local smoke-free legislation are from 11.8% at 2nd semester 2013 increasing to 17.2 at 1st semester, 25.9% at 2nd semester 2014, 37.8% at 1st semester 2015 and 42.0% at 2nd semester 2015. The smoking ban coverage is increasing from 21.2% to 77.8%. The 3 most violations of smoke-free policy at the third study are found cigarette butts indoor, providing ashtray indoor and smoking indoor. The factors associated the compliance to local smoke-free legislation are dissemination coverage, knowledge of managers and application of internal monitoring on the implementation of local smoke-free legislation.

Conclusions: The increasing of the compliance particularly in 2015 shows the acceleration of tobacco control (TC) programs in Bali such as the initiation of LSFL at districts/city level followed by dissemination, TC team building, signage and enforcements through random inspections and publish the results at mass media. A continuous dissemination, supervision and mentoring to managers of each smoke free area is needed to reach the target, 80% comply. Furthermore, developing an internal monitoring team in each area is an important point to monitor and ensure the compliance at their own building.

EP-222-29 Advancement of (tobacco) smoke-free environment in Karnataka: a comparative analysis

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Background: India is a home for 12% of the world's smokers and more than 1 million adults die every year in India due to tobacco use. Government of India has enacted smoke free rule under The Cigarettes and other Tobacco Products Act 2003 (COTPA) under which smoking is prohibited in all public places. Government of Karnataka taking serious note on this implemented the project 'Effective enforcement of

tobacco control laws by capacity building and monitoring' in all 30 Districts in Karnataka with support of Bloomberg philanthropy and The Union.

Methodology: Compliance survey were conducted before i.e. in the month of March 2013 and after i.e. in November 2015 the implementation of the project in the 10 Districts to assess the compliance of smoke free rules by using a structured, pre- tested checklist. By cluster sampling method total of 553 public places were observed.

Results: Before and after the implementation of Bloomberg initiative Project (2013 & 2015) as per the survey conducted by State Anti Tobacco Cell, Karnataka with technical support from The Union. As a result of effective implementation of smoke free rules, display of COTPA Section 4 Signage had been increased from 23.8% to 74 %, No smoking in public places has been increased from 63.3%, to 78.17% Smoking aids were not found in public places increased from 64.3% to 84.74%.

Conclusion: Over all, a majority of the places are complying to the section 4 of COTPA, and those who are following the norms are also abiding completely to the specifications as evident by the results. Approximately, more than one million people have been protected from passive smoke in Karnataka.

Table Comparative analysis

S.No	Indicators	Before implementation of BI Project (2013) %	After the implementation of BI Project (2015) %
1	Display of specified NO SMOKING signage	23.8%	74%
2	No active smoking observed	63.3%	78.17%
3	Smoking aids were not found	64.3%	84.74%
4	Absence of smell of cigarette or bidi	51.9%	74.28%

EP-223-29 Millennium youths joining hands for a tobacco-free generation

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Background and challenges to implementation: Majority of the youth's populations in Zambia live in high density communities and rural areas, which face high poverty levels and health disparities due to lack to education and healthcare services. Current economic situation in Zambia has left many populations vulnerable to unhealthy condition. Youths and Children sell cigarettes and other form of tobacco to meet their daily meals and school requirements and some do so as to peer pressure in the name of becoming 'cool'.

Intervention or response: In line with the 16th World

Conference on Tobacco or Health Youth Workshop, millennium children from five schools in Lusaka District born from year 2000 and above were drawn to participate in the commemoration of World No Tobacco Day 2015. To raise the voice of young people, Abu Dhabi Youth Workshop slogan of 'NO MORE TOBACCO IN THE 21ST CENTURY' was exhibited. Messages exhibited on the banners were messages of lobbying the government of Zambia to urgently implement the World Health Organization Framework Convention on Tobacco Control, ban tobacco advertising, promotion and sponsorship, more mass media campaigns on the harms of tobacco use, intensify curbing the illicit tobacco trade, and 100% smoke-free Zambia.

Results and lessons learnt: The commemoration was officiated by the Zambia Republican Vice President and covered by media houses both print and electronic. Zambia has a population of over 13 000 000 people. Over half the population got the anti tobacco messages. The government has set up a ministerial liaison committee to look into Illicit Trade of Tobacco Products. The five schools have formed Anti-tobacco Clubs.

Conclusions and key recommendations: The need to invest in young people to push the agenda of tobacco control is a goal for Zambia as youths are the engines of change.

- Youths are to be supported to join forces in developing a framework for prioritizing policies to protect them to achieve the goal of 'NO TOBACCO IN THE 21ST CENTURY'.

- Youths are to be supported both nationally and internationally to actively participate in monitoring and reporting tobacco industry tactics.

14. Latent TB infection: something for everyone

EP-224-29 Does the tuberculin skin test result vary by gender?

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Background: The response to purified protein derivative (PPD) when applying a tuberculin skin test (TST) reflects the adaptive immune system's ability to recognize *Mycobacterium tuberculosis* and subsequently activate the innate immune system. It has been shown that this response is impaired in patients with an insufficiently reacting immune system and a negative TST increases risk of death during treatment. Further, the immune system is different in males and

females due to genetic and hormonal differences. Estrogen stimulates Th-1 lymphocytes, the presumably most important cell in the response towards MTB, to increase Interferon- γ production. We compared verified tuberculosis (TB) patients' TST response at the beginning of treatment to see if it differed by gender.

Methods: Data from diagnosed TB patients started on treatment between 2003 and 2014 in Guinea-Bissau were analyzed. Odds ratios for positive TST, i.e. an induration with a mean of width and length ≥ 10 mm, crude and corrected for age, human immunodeficiency virus (HIV) infection, smear positivity and vaccination with Bacille Calmette Guérin (BCG) was assessed.

Results: Overall 1212 patients diagnosed with TB and having a TST done at treatment start were included in the study, 62% were male. Of the included patients 343 were HIV-infected, 36% of the females against 24% of the males ($P < 0.001$). Male patients had higher odds for a positive TST (crude OR 1.38 (95%CI 1.06 - 1.80)). When controlled for HIV, age, BCG scar and smear positivity the increased OR for males regarding a positive TST remained (adjusted OR 1.28 (95%CI 0.97 - 1.67)) though insignificant. Anergy towards PPD was more frequent in females (29% vs. 23%, $P = 0.017$) overall, but equally distributed among HIV uninfected patients (23% vs. 20%, $P = 0.389$). Among patients with anergy 14% died vs. 5% among PPD reactive patients ($P < 0.001$) - a result seen in both females (16% vs. 7%, $P = 0.003$) and males (13% vs. 4%, $P \leq 0.001$), irrespective of HIV status.

Conclusion: Male TB patients in our setting had less anergy towards PPD, which may indicate a stronger immune response compared to females or result from the higher HIV co-infection rate in female TB patients.

EP-225-29 Optimizing screening for latent tuberculosis infection among foreign-born persons in the United States using latent class analysis

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Background: Tuberculosis (TB) elimination in low-prevalence settings like the United States will require efficient strategies to screen for latent TB infection (LTBI) among high-risk groups, including persons born in high TB incidence countries. Identifying such strategies is hampered by the imperfect nature of available tests and the lack of a gold standard for LTBI diagnosis.

Design/methods: The TB Epidemiologic Studies Consortium is conducting a multicenter cohort study in the U.S. examining the performance of the three available tests for LTBI: tuberculin skin test (TST) and two interferon gamma release assays (IGRAs)- QuantiFERON Gold in-tube (QFT) and T-SPOT.TB (TSPOT). We performed a Bayesian latent class analysis on data from the first 8,126 foreign-born, HIV-seronegative participants 5 years of age and older. Standard U.S. cut points were used for TST interpretation; ≥ 5 spots was counted as positive for the TSPOT.

Results: Latent class analysis estimated LTBI prevalence of 28.8% in this cohort. The positive predictive value (PPV) of the TST was 54.8% (95% credible interval (95CrI) 53.0-56.6%); the PPV of the QFT and TSPOT were 91.3% (95CrI 89.6-92.9%) and 93.8% (95CrI 92.2-95.2%), respectively. A positive QFT with a positive TST had a PPV of 97.1%, whereas a negative QFT with a positive TST had a PPV of 12.3%. A positive TSPOT with a positive TST had a PPV of 98.0%, whereas a negative TSPOT with a positive TST had a PPV of 14.0%.

Conclusions: Based on latent class analysis in this large cohort of foreign-born individuals, the TST alone had poor PPV for LTBI; approximately half of persons with a positive TST did not have LTBI. Either of the IGRAs had high PPVs for LTBI. Combining either a QFT or TSPOT with the TST accurately discriminated infected from uninfected persons, with the caveat that tests were done simultaneously in our study so our data do not account for potential boosting of the QFT/TSPOT by prior TST. These results support both US guidelines preferring IGRAs in foreign-born persons who may have received BCG and European guidelines recommending use of the TST followed by a confirmatory IGRA for those with an initial positive TST.

EP-226-29 Evaluation of screening for latent tuberculosis infection among HIV-infected persons born in the United States using latent class analysis

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Background: HIV-infected persons with latent tuberculosis infection (LTBI) are at high risk for progression to tuberculosis (TB) disease; therefore guidelines recommend screening for LTBI in this population. Previous studies evaluating the diagnostic performance of available tests for LTBI in this population

report conflicting results and are limited by the lack of a gold standard test.

Methods: The TB Epidemiologic Studies Consortium is conducting a multicenter cohort study evaluating the performance of the three available LTBI tests: tuberculin skin test (TST) and two interferon gamma release assays (IGRAs) QuantiFERON Gold In-Tube (QFT) and T-SPOT.TB (TSPOT). Standard United States (US) cut points were used for TST and IGRA interpretation; ≥ 5 spots (including borderline results) were counted as positive for TSPOT. We performed a Bayesian latent class analysis (LCA), with data from US-born HIV-infected adults who had valid results for all three tests.

Results: Among 1,238 HIV-infected persons included, 795 (64%) had a non-missing self-reported CD4+ lymphocyte count (median 441 cells/mm³, interquartile range [IQR] 350-760). Using LCA, the estimated LTBI prevalence was 4.9% (95% credible interval [95CrI] 3.3-7.1%). The sensitivity, specificity, and positive predictive value (PPV) of the TST, QFT, and TSPOT can be found in the Table. While both IGRAs were significantly more sensitive than TST (95CrI for the sensitivity difference 16.5-49.6% and 1.0-33.5% for the QFT and TSPOT, respectively), only TSPOT was significantly more specific than TST (95CrI for the specificity difference 1.5-4.1%).

Conclusions: In this cohort of US-born HIV-infected adults, the estimated LTBI prevalence was similar to that found for the general US population by the National Health and Nutrition Examination Survey (NHANES) using two tests (TST and QFT-GIT). Both IGRAs were more sensitive than TST although only TSPOT was more specific than TST. These results suggest that the TST and QFT perform less well when compared to the TSPOT in this population of HIV-infected persons from a low-incidence TB setting.

Table Diagnostic performance of TST, QFT, TSPOT

	TST	QFT	TSPOT
Sensitivity	42.6%	76.5%	59.9%
(95% CrI)	(34.1-51.4%)	(60.3-90.3%)	(44.3-75.3%)
Specificity	96.5%	96.5%	99.2%
(95% CrI)	(95.3-97.5%)	(95.1-97.9%)	(98.4-99.9%)
PPV (95% CrI)	38.7%	53.3%	79.9%
	(26.7-52.5%)	(38.1-70.7%)	(61.7-96.8%)

EP-227-29 Controversies in the diagnosis and treatment of tuberculosis infection among pediatric infectious disease specialists in North America

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Background: The degree to which advancements in the diagnosis and treatment of tuberculosis infection

(TBI) have been integrated into practice by pediatric infectious disease (PID) specialists is unclear.

Methods: In late 2015, we conducted an online survey of the Infectious Diseases Society of America's Emerging Infections Network (EIN) membership querying PID specialists about TBI testing and treatment.

Results: 197/323 (61%) members responded. 93% care for < 5 children with TB disease and 66% for < 5 children with TBI annually. We identified substantial variation in use of interferon gamma release assays (IGRAs) based on a child's age, immune status, and TB risk factors. Tuberculin skin test (TST) use is more common in preschool-aged children than older children (OR 3.2, 95%CI 2.1-5.1). Only 7% of providers reported using IGRAs in all ages. There was no consensus for the TST induration above which providers would *not* obtain an IGRA. Almost 50% stated they obtain IGRAs in children with TST results ≥ 15 mm of induration but only 9% would do so for children with TSTs > 20 mm. Variation exists in the management of children with discordant TST and IGRA results. For BCG-immunized children with positive TST and negative IGRA results, providers are more likely to treat for TBI if children are younger (OR 2.8; 95%CI 2-3.9) or have larger TST indurations (OR 3.4; 95%CI 2.4-4.8). Less variation exists in TBI treatment, with 86% preferring 9 months of isoniazid and few providers using newer or shorter treatment regimens. Providers are more than twice as likely to seek advice from organization guidelines as from the scientific literature, but these guidelines are often not followed.

Conclusions: Substantial variation exists in the diagnosis and management of TBI; uptake of newer diagnostic tools and recommended treatment regimens has been slow among PID specialists. Variation in practice and the lag time for integrating new recommendations into practice may indicate the relative infrequency with which providers encounter TBI and TB disease. Our findings reflect the need for increased visibility and dissemination of existing TB management guidelines, and access to resources for expert consultation for scenarios not covered by guidelines.

EP-228-29 LTBI screening in NW England: evaluating experience from almost two decades

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Introduction: Rates of tuberculosis (TB) in England remain comparatively high. About three quarters of TB cases in the UK occur amongst non-UK born individuals, often as a result of reactivation of latent TB infection (LTBI). Programmatic testing and treatment for LTBI is a key intervention of the Collaborative TB strategy for England. This paper aims to review the evidence of a long-standing LTBI screening initiative in England to shape and inform policy around LTBI screening.

Methods: A retrospective cohort was created through probabilistic linkage between LTBI screening data and TB case data from the Enhanced TB surveillance system in the UK. Persons screened for LTBI in Blackburn were followed up until they died, became a case, imputed emigration date or cohort end date (end of 2014). Incidence rates (IR) and incidence rate ratios (IRRs) of TB were calculated in single and multi variable (Poisson regression) analysis.

Results: In total, 21 of the 1,341 individuals screened with QuantiFERON (QFT) between 2009 and 2013 and 76 of 479 screened with Tuberculin skin test (TST) between 1989-2001 were reported with active TB. Crude incidence rates (IRs) amongst LTBI positive, treatment naïve individuals were 4,900 per 100 000 person years (py) and 2,297 per 100 000 py in the QFT and TST cohorts respectively. Poisson regression showed that LTBI positivity (IRR 27.0, 95%CI 8.5- 86.2) and no chemoprophylaxis (IRR 0.14, 95%CI 0.04-0.5) were associated with becoming a case of TB.

Conclusions: Our study demonstrated the feasibility of LTBI screening and treatment and provided estimates of effectiveness in the prevention of TB case reactivation in an observational cohort with long-term follow up. It showed high TB rates among treatment naïve individuals and a strong association between LTBI positivity and absence of treatment with TB case notification. Important policy lessons can be drawn from this cohort to inform national LTBI screening in England and beyond.

EP-229-29 High prevalence of latent TB infection among non-household contacts in urban Uganda

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Background: Although tracing, identifying, and investigating individual contacts of infectious TB cases is a key aspect in TB control, it is not routinely done in high TB incidence settings. As part of an ongoing social network study on transmission of TB in Kampala Uganda, we examined the relationship between contact status and household exposure on latent TB infection (LTBI) prevalence.

Methods: In a cross-sectional study, we identified Index TB cases and enrolled their household (HH) and non-household (NHH) contacts. For each index TB case, we identified an age- and sex-matched non-TB control and enrolled their contacts as well. We estimated the prevalence of LTBI among both HH- and NHH- contacts of TB index cases and non-TB controls. LTBI was defined as induration of ≥ 10 mm on tuberculin skin test.

Results: Of the 957 contacts enrolled, 521 (54%) were male, with mean age 26 (± 12) years. 483 (50.5%) contacts came from 80 TB index cases while 474 (49.5%) contacts were from 77 non-TB controls. HH contacts were 187 (39%) from TB cases and 103 (22%) from non-TB controls. Among all contacts, LTBI prevalence was 43% (95%CI 40-46%). When we stratified by household and TB status, LTBI prevalence was highest in HH contacts of TB cases and lowest in HH contacts of non-TB controls (56% vs 34%, $P=0.0004$). LTBI prevalence was also surprisingly higher in NHH contacts of non-TB controls than NHH contacts of TB cases (42% vs 38% respectively), although comparable between the two groups ($P=0.27$).

Conclusions: The prevalence of LTBI was high among NHH contacts of non-TB controls. This may be partly explained by a high background level of TB infection in this urban setting. Understanding assortment patterns among contacts of TB and non-TB cases may provide further insight into where TB transmission is more likely to occur and inform effective TB control.

EP-230-29 The incidence of active tuberculosis correlates geographically with the prevalence of latent tuberculosis infection in a high-incidence urban setting

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Introduction: The World Health Organisation recommends the routine investigation of at-risk groups for Latent Tuberculosis (LTBI) in high income countries. Since April 2014, The London Borough of Newham has tested 5464 recent migrants for LTBI in a community based screening programme using an Interferon Gamma-Release Assay (IGRA) as part of Public Health England's (PHE) national strategy. We considered whether the prevalence of LTBI amongst recent migrants correlated geographically with the incidence of active TB in Newham, and if therefore active TB incidence is an appropriate proxy measure for guiding public health policy on LTBI.

Methods: A retrospective study of geospatial case distribution in Newham GP surgeries comparing active TB cases (2012-2014) from the national registry held by PHE to IGRA positive cases (April 2014-December 2015) from the community LTBI programme. LTBI cases found through contact tracing were not included. Case numbers were adjusted for surgery size for estimates of incidence and prevalence. GP surgeries that had not offered LTBI screening were also excluded.

Results: 52 of the 62 GP surgeries (84%) within Newham were included in the analysis. The mean estimated LTBI prevalence per GP surgery was 259/100 000 (95%CI 180-337). The mean estimated active TB incidence per GP surgery was 60 per 100 000 patients per year (95%CI 47-72). Initial analysis, after log transformation, confirmed our assumptions of normality and linearity. We investigated the relationship between rates of active TB and IGRA positivity using a Pearson correlation coefficient and linear regression. There was a strong positive correlation between the two variables ($r=0.549$, $P<0.001$) (Figure).

Conclusions: The incidence of active TB correlates geographically with the prevalence of LTBI amongst recent migrants in a high TB-incidence urban setting in the UK. Screening and treatment for LTBI in migrants is essential to reduce TB incidence in the UK.

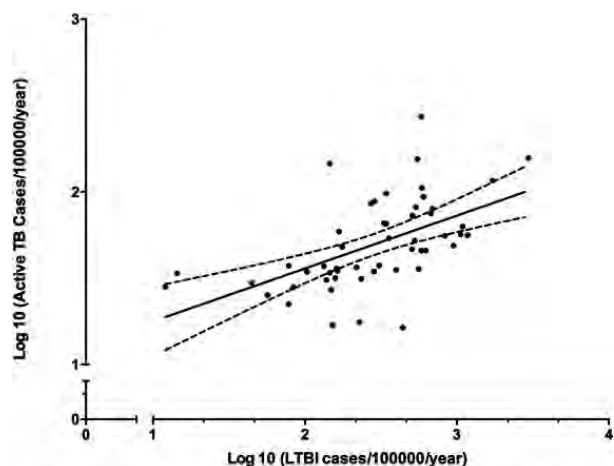


Figure: linear regression comparing cases of Latent Tuberculosis Infection (LTBI) (2014-2015) per 100,000/year and active Tuberculosis (TB) (2012-2014) per 100,000/year for General Practice Surgeries in the London Borough of Newham. ($r^2=0.30$, $p<0.00001$, $n=52$)

EP-231-29 Toward safe and reachable preventive therapy for LTBI: a multicenter randomized controlled study in Taiwan

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Background: By incorporating long-acting rifapentine, a new regimen combining weekly rifapentine and high-dose isoniazid for a total of 12 doses (3HP) has been proven of equal potency and similar toxicity with a much higher completion rate than daily isoniazid for 9 months (9H). However, such study is lacking in Asia, the high endemic area of TB.

Methods: The study was conducted since August 2014 in four hospitals in Taiwan. We prospectively enrolled close contacts aged ≥ 12 with positive tuberculin skin test. Chest radiography and sputum studies, if necessary, were performed to exclude active pulmonary TB. Participants were randomized into 2 groups with different preventive regimens. The primary outcome is treatment completion rate of the two preventive regimen. The secondary outcome is toxicity. All participants were followed for 2 years and screen for the development of active pulmonary TB by chest radiography and sputum studies if necessary.

Results: Up to Oct. 23, 2015, a total of 210 cases were enrolled. The mean age was 31.7 ± 15.1 and 55.2% were male. A total of 104 and 90 cases in the 3RH and 9H groups, respectively, entered into this analysis. The clinical characteristics were similar between the two groups. The pre-treatment hemo-

gram and biochemical data were also similar. Hepatotoxicity was more common in the 9H group than in the 3RH group. Though not significant, risk of significant hepatotoxicity was higher in the 9H group (4.3% vs. 1.0%, $P = 0.184$). Among the 194 cases, preventive therapy was discontinued in 29, including 11 in the 3RH group ($P = 0.066$). The incidence rate of any adverse events is significantly higher in the 3RH group (46.2% vs. 28.9%, $P = 0.014$).

Conclusions: The study is currently ongoing. Present data show that the adherence rate for 3-month rifapentine plus high-dose isoniazid is likely to be higher than that for 9-month isoniazid. Though the former regimen is more likely to have flu-like symptoms and malaise, they are usually well-tolerated, mild, and transient. In addition, risk of liver function impairment is lower for the former regimen.

EP-232-29 Improved tuberculosis contact investigation and isoniazid preventive therapy among under-5 children in two regions of Ethiopia

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Background: IPT is indicated for under-five children who have a history of contact with a sputum-smear-positive (SS+) pulmonary TB case, after ruling out active TB disease. There has been minimal progress in its implementation despite the global and national recommendation. This analysis was aimed at describing the progress of IPT uptake among under-five children in two regions of Ethiopia. The routine report does not include IPT completion data and it is not presented here.

Intervention: The USAID-funded HEAL TB project in collaboration with the Amhara and Oromia Regional Health Bureaus (RHB) has been implementing contact screening of SS+ pulmonary TB index cases and IPT for eligible children. The project supported the training of health managers and health workers on childhood IPT, provided job aides, strengthened mentoring, and established monitoring mechanisms.

Results and lessons learnt: There were 9864 under-five children registered as household contacts of SS+ pulmonary TB index cases. Of these, 9145 (92.7%) were evaluated for active TB and presumptive TB was identified among 517 (5.7%) children. Of 8628 children eligible for IPT, 3094 (35.9%) received IPT and there was no regional variation. The IPT uptake in 2014/15 was 3.5 times that of 2012/13 (12.4% to 42.8%) [See Table]. The comprehensive support provided to health managers, health workers, men-

torship and close monitoring resulted in a significant improvement in uptake of childhood IPT. To address the lack of complete data regarding childhood IPT in the routine reports, a childhood IPT register was developed that is currently approved by the RHBs.

Conclusion: Contact screening is a very good entry point for childhood IPT. The project started the initiative of IPT and it showed a significant improvement over three years, though the IPT uptake still needs improvement.

Table IPT coverage for under-5 children

Variable	2012/13 n (%)	2013/14 n (%)	2014/15 n (%)	Total n (%)
Close contacts, under-5 children	528	3508	5828	9864
Under-5 children evaluated for TB	457 (86.6)	3097 (88.3)	5591 (95.9)	9145 (92.7)
Under-5 children eligible for IPT (screen negatives)	442	2,796	5390	8628
Under-5 children started on IPT (% IPT coverage)	55 (12.4)	732 (26.2)	2307 (42.8)	3094 (35.9)

EP-233-29 LTBI treatment completion and risk factors for non-completion in an urban city of western Canada: a population-based study

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Background: Latent Tuberculosis Infection (LTBI) treatment is provincially funded and free to all individuals diagnosed with LTBI. Information on the geographical distributions of LTBI cases, service providers, and treatment completion is critical for service planning, resource allocation and program evaluation.

Objectives: The objectives of this study were 1) to describe the epidemiology of LTBI treatment completion and 2) to identify risk factors associated with treatment non-completion in an urban setting in western Canada.

Methods: A population-based retrospective cohort study design was used. The provincial Drug Program Information Network database (2011-2014) was used to extract all individuals (LTBI cases) who received isoniazid (INH) or rifampin (RFP) as the first and only prescription, and not combined with other antibiotics. Treatment completion was defined as being dispensed 12 months (≥ 270 days) of INH or 6 months (≥ 120 days) of RFP, excluding children who were dispensed INH for window period prophylaxis. Descriptive statistics were used to illustrate the geographical and demographic distribution of LTBI cases. Logistic regression models were employed to

evaluate the associated factors for failure to complete LTBI treatment.

Results: A total of 744 individuals were dispensed INH or RIF for LTBI treatment during the 3-year period. 585 (79%) were dispensed INH and 159 (21%) were dispensed RFP. Half of the LTBI cases resided in two areas (*core area and northern quadrant*) of the urban centre. A total of 525 LTBI cases (73%) completed treatment. The completion rate was higher in females (75.8%) than in males (68.8%). Paediatric LTBI cases had the highest completion rates (89%), followed by those dispensed by nurse practitioners (84%). Non-completion is associated with prescribers managing less than 10 cases over 3 years (OR=6.6, 95%CI 4.0 - 10.8) and residing in core area (OR=1.5, 95%CI 1.0-2.2).

Conclusion: Children LTBI cases and those dispensed by nurse practitioners had optimal treatment completion. Factors associated with non-completion were prescribers' case load and living in the core area. This data is shaping program decisions around LTBI treatment within the urban centre. Further investigations on the characteristics of prescribers (clinics/centres) with high LTBI completion rates are required for program planning and resource allocation.

EP-234-29 Dynamics of progression to active tuberculosis: which model structure to best replicate them?

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Background: Tuberculosis (TB) latency dynamics present a specific pattern with a higher risk of disease activation in the early stages of infection but a life-long risk of disease often stated to be around 10%. This pattern significantly varies according to the age at infection. Inclusion of TB-latency is necessary for models to capture transmission dynamics and to accurately inform policies. Different structures are used in modern TB models while it remains unclear whether they are all capable of reproducing the activation dynamics empirically observed.

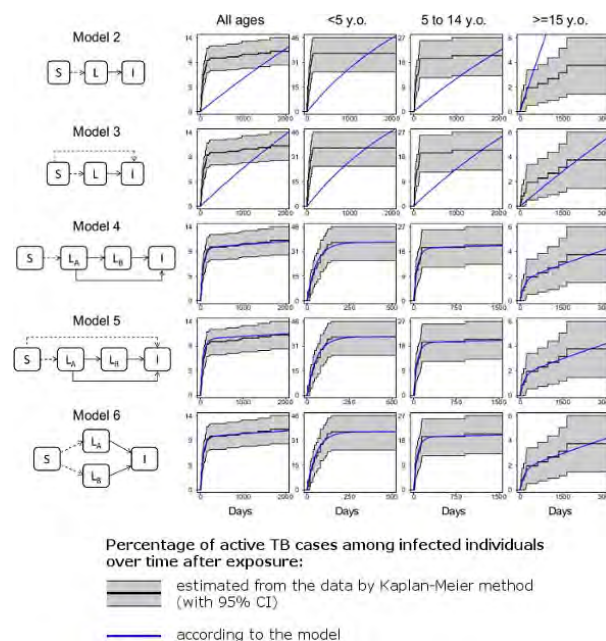
Methods: We reviewed 95 articles related to TB-modelling and classified them according to the latency structure used. We then fitted the different models to the activation dynamics observed from 613 infected contacts diagnosed in Victoria (Australia), including 67 active cases. Fitting was performed using three age categories. We used two independent fitting

methods: Least-Squares-Optimisation (LSO) and Maximisation of a Survival Likelihood (MSL).

Results: We obtained six different model structures from our literature review. Among them, only three were capable of reproducing the activation dynamics empirically observed (Models 4, 5 and 6) while the three others provided very poor fitting to the data. This same result was observed regardless the age category. Model 5 led to the same fitting scores as Models 4 and 6, but involved estimating more parameters. Results obtained from both the LSO and MSL methods were strongly concordant (Figure). Model 1 (not represented) employs no latency compartment and is not compatible with the data.

Conclusions: Only the models employing two latency compartments are able to reproduce TB latency dynamics accurately. These two compartments may be positioned either in series or in parallel, both demonstrating excellent predictions. Using a single (or no) latency compartment in a TB model results in poor predictions and may lead to misguidance for TB-control policies.

Figure Fitting of the six models to the data (MSL method)



ORAL ABSTRACT SESSIONS

21. The Union/CDC late-breaker session on TB

OA-3032 Effective TB case finding with routine systematic cough screening in general outpatient, in-patient HIV clinical services in Haiti, 2012–2015

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Background: Haiti has the highest rates of tuberculosis (TB) in the Western hemisphere, with WHO estimates of 244/100 000 persons and 200 new infections per 100 000 persons/year. TB disease detection in Haiti relies primarily on passive case-finding of individuals presenting to health facilities with characteristic symptoms. In an effort to improve case detection and TB infection control in the wake of the 2010 earthquake, the National TB Program implemented systematic cough screening across all designated TB diagnostic and treatment facilities in the country, including general outpatient, inpatient and HIV clinical services.

Methods: We analyzed routine aggregate program data from January 2012 to December 2015 from 110 health facilities providing comprehensive TB and HIV clinical services; these facilities annually notify ~80% of new TB cases in Haiti. Data included the number of patients who were evaluated for cough (TB suspects), the number of TB suspects who underwent sputum smear microscopy for acid-fast bacilli (AFB), and the number of TB suspects who had smear-testing and positive smear microscopy, as well as the geographic location of notifying health facilities.

Results: Overall, 215 525 TB suspects were evaluated during the period. Of those, 191 748 (89%) patients underwent sputum smear microscopy for AFB, and 29 008 (15%) TB suspects had a positive smear for AFB. The yearly percentages of patients with positive smear for AFB were 16.2%, 15.1%, 14.2%, and 15.6%, respectively, for 2012, 2013, 2014, and 2015. Three geographic departments - West, North, and Artibonite - represented 63% of the sputum AFB positive TB cases.

Conclusions: In the post-earthquake period, we observed persistent high rates of smear-positivity among TB suspects identified by routine systematic cough screening. These findings suggest sustained TB transmission levels, underscoring the importance of further strengthening current TB control efforts. Use of this case-finding approach should be expanded in

order to reduce delays in diagnosis and improve treatment outcomes and overall TB control in Haiti, and may be impactful in other resource-constrained settings.

OA-3097 Performance of Xpert® MTB/RIF in previously treated patients for the diagnosis of tuberculosis in a highly endemic setting

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Background: Several studies suggest that false-positive Xpert® MTB/RIF results are more frequent in previously treated TB patients (PTP).

Method: To further evaluate the Xpert performance in PTP versus non-PTP, we investigated during one year all inmates in Rio de Janeiro prisons (TB prevalence > 5%) initially diagnosed as pulmonary TB on the basis of AFB sputum smear-positivity or, in smear (-) cases, X-ray evidence of TB. Sputum samples were tested by Xpert and cultivated. The final diagnosis of smear (+)/culture (-) cases was established by comparing initial and follow-up X-rays under TB treatment.

Results: Of the 420 cases diagnosed, 140 were PTP (33.3%) with, for 133, information on time since the end of previous treatment: > 2 years for 72 (54.1%), 1 to 2 years for 49 (14.3%), < 1 year for 42 (31.6%). Taking as reference a composite standard (culture or, in 11 TB-negative cases, response to treatment), the Xpert sensitivity, specificity and PPV were 90.9%, 85.7% and 99.2% respectively for PTB versus 92.3%, 100.0% and 97.5% for non-PTP. Out of the 12 Xpert (+)/culture (-) PTP, 4 were recent defaulters who stopped their treatment 2 to 3 months before entering the study, 8 had a very low Xpert positivity rate and 9 had patchy infiltrates in upper lobes which improved under treatment. Overall, only one result was considered Xpert false (+): a PTP patient cured 3 years before who had a bronchitis, fibrotic lesions on the right upper lobe, similar to those observed at the end of the previous TB treatment, and which did not improve under the actual treatment.

Conclusions: Our study based on bacteriological and, unavailable in most previous studies, X-ray follow up, showed optimal performances of Xpert in PTP and call for its unrestricted use for TB diagnosis, even in previously treated patients.

Table Xpert® MTB/RIF results according to tuberculosis

TB diagnostic criteria	History of TB treatment (n=140)		No history of TB treatment (n=280)	
	Xpert (+) (n=122) n (%)	Xpert (-) (n=18) n (%)	Xpert (+) (n=252) n (%)	Xpert (-) (n=28) n (%)
Culture (+)	110 (90.0)	17 (22.2)	230 (91.3)	6 (21.5)
Smear (-)/ culture (-) with X-ray improvement under TB treatment	11 (9.0)	8 (44.5)	22 (8.7)	15 (53.5)
Smear (-)/ culture (-) without X-ray improvement under TB treatment	1 (0.8)	6 (33.3)	0	7 (25.0)

OA-3114 Tuberculosis stigma in a high-risk indigenous population in Brazil

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Background: The Guarani-Kaiowá is Brazil's second-largest indigenous group. Average annual tuberculosis incidence rates among the Guarani-Kaiowá are 325/100 000 in the district of Amambaí in the Brazilian state of Mato Grosso do Sul (MS), ten times the national average. Although stigma is acknowledged as an important factor for tuberculosis management in indigenous communities, few publications have investigated tuberculosis stigma among indigenous populations. This study aims to understand the perception of tuberculosis and the role of tuberculosis stigma among the Guarani-Kaiowá.

Method: Using semi-structured questionnaires, we interviewed adult men and women in 4 indigenous villages around Amambai, MS. We identified cases from a registry previously made for another study. Non-cases were randomly selected, and matched by age, sex, and village of residence. The interviews were conducted in Guarani and Portuguese, and analyzed using NVivo.

Results: Of 39 interviews, 18 were cases (7 men, 11 women) and 21 non-cases (10 men, 11 women). The primary explanations given for contracting tuberculosis were starvation, contaminated food and water, and as a sequela of accidents or domestic violence. Patients would not mention their tuberculosis diagnosis outside the family, isolated themselves and/or were shunned by the community during treatment. Patients experienced this as a traumatizing rejection. 95% of patients used traditional medicine for several months before seeking antibiotic treatment. Men reported delaying seeking treatment for fear of losing their jobs. In several instances, the healthcare

personnel erroneously told patients to eat and sleep separated from family.

Conclusions: Although tuberculosis was perceived as an infectious disease, no respondents could explain the transmission mechanism. Fear of contracting tuberculosis was widespread and led to isolation of tuberculosis patients. Tuberculosis was not perceived as associated with indecent behavior as observed elsewhere, perhaps because co-infection with HIV is rare in this population. However, the isolation caused feelings of guilt and lack of self-worth in patients. Our findings suggest that stigma plays a significant role in delaying treatment, thus contributing to the continued transmission of tuberculosis in the community. The stigmatization of tuberculosis was rooted in a unclear understanding of TB transmission, often a result of incorrect orientation by the health-care service.

OA-3117 Interim results of Nix-TB clinical study of pretomanid, bedaquiline and linezolid for treatment of XDR and treatment intolerant/failed MDR-TB

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Background: Patients with extensively drug-resistant (XDR) tuberculosis (TB) have had limited options for treatment and high mortality. Nix-TB is an ongoing open label study at two South African sites of bedaquiline (400 mg daily for 2 weeks followed by 200 mg three times a week), pretomanid (200 mg per day) and linezolid (1200 mg per day) given orally for 6 months with the option to extend treatment to 9 months for participants who do not culture convert within 4 months.

Method: The primary endpoint is bacteriologic failure or relapse or clinical failure at 6 months after the end of treatment. Extensive clinical and laboratory and sputum liquid culture evaluations are performed at baseline and weeks 1, 2, 4, 6, 8 and then every 4-6 weeks through the end of treatment. Participants who complete treatment are followed closely for 24 months after the end of treatment with repeat clinical assessments and sputum cultures. This interim analysis includes the results of the first 15 patients who will have completed 6 months of post-treatment follow-up.

Results: Since April 2015 42 participants (80% with XDR-TB, 20% MDR treatment intolerant or failures) have been enrolled as of July 1, 2016. Of the 15 participants in the interim analysis 7 were HIV-

positive (47%). Two died from autopsy-confirmed disseminated multi-organ TB at 4 and 7 weeks after enrollment and 1 died from gastrointestinal bleeding related to erosive candida esophagitis 7 weeks into treatment. The remaining 12 completed 6 months of therapy. The majority was culture negative by week 8 and no patient needed an extension of treatment. The expected linezolid toxicities of peripheral neuropathy and myelosuppression were manageable, although the majority of participants required either reductions of dose and/or interruptions in linezolid dosing, as allowed by the protocol, during the 6 months of treatment. As of 1 July 2016, there have been no clinical or microbiological relapses.

Conclusions: Early results of this greatly simplified and shortened all-oral regimen for drug resistant TB appear encouraging in terms of both efficacy and safety.

OA-3161 Mutations in *pncA* are associated with poor treatment outcomes in MDR-TB patients in the Preserving Effective TB Treating Study (PETTS)

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Background: Pyrazinamide is a prodrug that plays a critical role in first and second-line tuberculosis treatment regimens. Mutations in the promoter and coding region of *pncA* in *Mycobacterium tuberculosis* are associated with resistance to pyrazinamide, and clinical samples contain a plethora of mutations within *pncA* with no apparent hot-spot. The Preserving Effective TB Treatment Study (PETTS) was a prospective observational study of multidrug-resistant (MDR) tuberculosis (TB) treatment and outcomes carried out in 9 countries in 2005-2010. We sequenced *pncA* and its promoter region from 914 *M. tuberculosis* isolates collected from individual patients enrolled in PETTS to evaluate the variety of *pncA* mutations, and additionally, we correlated *pncA* alleles with patient outcomes.

Methods: The entire *pncA* gene and 81-bp upstream were amplified and sequenced. Sequences were aligned to H37Rv using DNASTAR Lasergene 12 SeqMan Pro. For some amplicons, additional sequencing was performed using internal primers.

Results: *pncA* sequence data was obtained for all 914 samples. Twenty-seven percent of samples had a wild-type (WT) *pncA* gene, 51% had one or more single nucleotide polymorphisms (SNP), 18.3% had an insertion or deletion (indel) and 3.8% had promoter mutations. Among samples, 171 unique SNPs were identified in 73 of the 187 *pncA* codons. The presence of a WT *pncA* was associated with cure in 54.6% of individuals, while the presence of a SNP, indel or

promoter mutation was associated with cure in 46.4, 30.5 and 40.6% of individuals respectively. Conversely, WT *pncA* was associated with treatment failure or death in 12.4% of individuals while presence of a SNP, indel or promoter mutation was associated with failure or death in 26.6, 47.9 or 25% of individuals, respectively.

Conclusions: Analysis of *pncA* sequences from 914 MDR isolates identified a large variety of *pncA* mutations distributed throughout the gene. Presence of a non-WT *pncA* allele was associated with a non-favorable patient outcome.

OA-3163 Short-course MDR-TB treatment compared with standard of care in Uzbekistan: culture conversion rates after 2 months

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Background: Multidrug-resistant tuberculosis (MDR-TB) treatment is lengthy, toxic, and poorly effective. New WHO guidelines recommend a short-course regimen (SCR). Evidence for factors associated with successful SCR outcomes is limited, especially in contexts with high second-line resistance. Early culture conversion is important for treatment success and infection control. We compared 2-month, culture-conversion results from a single-arm, prospective, observational study of the SCR with patients treated with the international standard of care (SOC). **Method:** SCR study data (September 2013-March 2015) were compared with SOC data (September 2013-September 2015) from patients in different districts to SCR areas. Inclusion criteria were: MDR-TB diagnosis by culture and drug susceptibility testing; and > 2 months of treatment. Analysis exclusion criteria were: previous second-line drug treatment for >1 month; and fluoroquinolone resistance. Multivariate logistic regression estimated the association between SCR and culture conversion by 2 months while adjusting for credible confounding variables. Ethics approval: MSF and Uzbekistan Ethics Review Boards.

Results: 76 SCR and 224 SOC patients were included. Both groups were similar for gender, X-ray cavities, and body-mass index. In the SCR group, a higher proportion of baseline smear results were negative (46% vs 28%, $P < 0.001$) and a lower proportion had pyrazinamide resistance identified (57% vs. 72%, $P = 0.008$). 56 (74%) SCR patients achieved culture conversion by 2 months, compared with 114 (51%) SOC. Factors positively associated with culture conversion were: SCR vs SOC (aOR 2.04, 95%CI 1.11-3.76, $P = 0.022$); and female gender (aOR 1.78, 95%CI 1.09-2.93, $P = 0.022$). Higher baseline smear-

positivity was negatively associated with conversion: aOR 0.50 (95% CI 0.28-0.90) and 0.22 (95% CI 0.11-0.43), for smear scanty/1+ and 2/3+, respectively, compared with negative. There was a weak negative association with increasing age: for every 10 years from age 5-15 years (aOR 0.99, 95% CI 0.97-1.00, $P=0.060$). Baseline resistance to ethambutol, pyrazinamide, and kanamycin were not associated with conversion and removed from the model.

Conclusions: There was a two-fold greater odds of culture conversion by 2 months with the SCR. This study is limited by being a retrospective cohort comparison. The higher OR of culture conversion suggests introduction of the SCR could reduce transmission in this subgroup of MDR-TB patients.

22. Priorities in finding the missing cases

OA-445-29 Delay in diagnosis of pulmonary tuberculosis in low- and middle-income settings: systematic review and meta-analysis

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Background: Assessment of diagnostic delays is essential to evaluate effectiveness of control programs, and identify programmatic impediments. Thus, we have reviewed recent studies to summarize patient, health system and total delays in diagnosis of pulmonary tuberculosis and associated factors with it in low- and middle- income countries.

Methods: The review was done following standard procedures of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement and checklist. Web-based databases were searched to retrieve relevant studies from 2007 to 2015. Studies included were cross-sectional, case-control and cohort designs, if participants were adult pulmonary tuberculosis patients who presented self at health facilities. The median delay was summarized using median, box plots, inter quartile ranges, 95% confidence interval and ranges. Both random and fixed effect models were used to combine odds ratios in the meta-analysis by comprehensive meta-analysis software.

Results: Forty studies involving 18,975 patients from 27 countries qualified for systematic review and 14 for meta-analysis. The median total delay ranged from 30 to 367 days; with relatively more for patient delay (4 to 199 days) compared to health system delay (2 to 129 days). The key determinants of patient delay included: poor literacy, long distance to health facility, evil/bad luck perception as cause, poor

knowledge of TB symptoms, first care seeking at informal providers, self-medication, pulmonary comorbidity and mild severity of illness. Good functional status, unusual symptoms, first care seeking at private and low level facilities, normal chest X-ray and smear negative results were key determinants of health system delay. The meta-analysis of 11 studies involving 4,371 patients showed that 42% of pulmonary tuberculosis patients delayed by a month or more; illiterate patients (pooled OR 1.5, 95% CI 1.1-1.9) and those who sought care first from informal providers (pooled OR 3.0, 95% CI 2.3-3.9) had higher odds of patient delay.

Conclusions: Delay in diagnosis is still a major challenge of TB control and prevention programs in low income setting. Efforts to develop new strategies for better case-finding strategies, and improving patients' care seeking behavior, service expansion and more sensitive diagnostic tools need to be intensified.

OA-446-29 Prolonged delays to diagnosis despite availability of free health services: a study of 76 486 tuberculosis patients in Yunnan, China

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Background: Delay in treating active tuberculosis impedes tuberculosis control by allowing ongoing transmission, and may explain the unexpectedly modest declines in global incidence. While China has achieved global targets of 100% DOTS coverage and 70% case-detection, there is evidence of prolonged delay before patients are identified and correctly treated at government health facilities. This study addresses two questions: do delays in initiating treatment persist despite full implementation of the DOTS strategy and a well-functioning tuberculosis control programme? And which patient groups are at higher risk of experiencing the delays to treatment initiation?

Methods: Electronic records of 76,486 adults diagnosed with smear-positive pulmonary tuberculosis between 2006 and 2013 in all 129 Centre for Disease Control (CDC) diagnostic units covering Yunnan province were analyzed. Delay was calculated at three stages: periods between 1) Self-reported symptom onset and identification at a CDC unit, 2) Identification at a CDC unit and confirmation of smear-positive tuberculosis 3) Confirmation and initiation of treatment. A cross-sectional analysis

was conducted to investigate the distribution of delays, followed by a nested case-control study comparing characteristics of individuals experiencing delays of more than 90 days between symptom onset and identification at a CDC unit (prolonged delay, cases) and less than 30 days (controls).

Results: The median delay to first identification at a CDC unit following symptom onset was 57 days (IQR 25-112), the largest contributor to total delay. Median delay to confirmation of smear-positive tuberculosis following identification at a CDC unit and to initiation of treatment following diagnosis was 2 days (IQR 1-6) and 1 day (IQR 0-1) respectively. Prolonged delay to first identification a CDC unit was associated with female sex, age group above 15-24 years, being a farmer, being a non-resident and belonging to specific ethnic groups.

Conclusions: Our results demonstrate that prolonged delays in diagnosis of infectious smear-positive tuberculosis patients occur even when the entire population is covered by free health services and case-detection targets are being met. Policies that focus on reducing delays in treatment of vulnerable groups, rather than only on increasing overall case-detection rates, may result in greater progress towards reducing tuberculosis incidence.

OA-447-29 Improved TB screening via a novel mHealth app in both the community and health facility settings in South Africa

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Background: Many people with TB are missed by health services in South Africa, particularly in rural areas where access is a key issue. The lack of systematic screening in health facilities also leads to missed diagnoses among those already seeking care. A program of active TB screening in health facilities and the community was implemented in Ugu District (population 722,000) to address these challenges.

Methods: Trained health screeners were placed in the outpatient department of 19 health facilities across Ugu District. Each screener was given a smartphone pre-loaded with an open source mHealth app to facilitate data collection and a monthly mobile package containing 30-35 minutes of airtime and 280 MB of data. Screeners identified people with presumed TB, collected good-quality sputum samples, and ensured linkage to treatment. Sputum collection was aided by an animated instructional video pre-loaded onto the smartphones in 5 languages. Screeners received a basic stipend supplemented

by performance-based incentives (Table). Community screening activities commenced three months after facility screening using the same mHealth app and a modified incentive plan.

Results: Over 15 months, 83 977 people were verbally screened for TB symptoms in health facilities, resulting in the identification of 30 503 (36.3%) people with presumed TB, the testing of 16 533 (54.2%) sputum samples and the detection of 1193 (7.2%) TB patients. Over 12 months, 10 906 people were verbally screened in the community, resulting in the identification of 4184 (38.4%) people with presumed TB, the testing of 3892 (93.0%) sputum samples and the detection of 145 (3.7%) TB patients.

Conclusions: The dual strategy of systematic screening in health facilities and active community case finding detected many TB patients previously missed by health services. The mHealth app greatly improved screener efficiency and allowed them to self-direct their work in order to maximize TB detection and thus the incentives they could receive.

Facility Incentive Scheme				
	Incentive	Frequency of Incentive	Range	Amount
1	Basic Stipend	Monthly	---	ZAR 1000
2	Screening Incentive	Monthly	280 - 319 Individuals Screened 320 - 350 Individuals Screened 351 or more Individuals Screened	ZAR 100 ZAR 150 ZAR 200
3	Sputum Collection Incentive: Percentage of presumptive cases that provide a sputum sample	Monthly	75% - 84% 85% - 94%	ZAR 100 ZAR 150
4	Data Quality Incentive: Percentage of results entered into the screening app	Monthly	75% - 79% 80% - 84% 85% - 100%	ZAR 100 ZAR 150 ZAR 200
Community Incentive Scheme				
	Incentive	Frequency of Incentive	Frequency of Payment	Amount
1	Day Rate: Paid for each day worked	Daily	Monthly	ZAR 20
2	Screening Bonus: Paid for each day that the screener screened more than 30 individuals	Daily	Monthly	ZAR 10
3	Sputum Sample Incentive: Paid for each sample delivered to the clinic WITH a positive or negative result from the laboratory	Daily	Monthly	ZAR 4
4	Positive Case Notification WITH Treatment Initiation: Paid for each TB case found in the community that was initiated on treatment at the local health facility	Monthly	Monthly	ZAR 200

Table Overview of incentive schemes

OA-448-29 Engaging private health care providers in Pakistan to increase case notification

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Background and challenges to implementation: Pakistan has the fifth highest TB burden in the world. Each year more than half a million people develop TB in the country. During 2013-14, around 300 000 TB cases were diagnosed leaving 227 000 (44%) patients undiagnosed and untreated. These 'missing' TB cases are a cause of great concern as they are likely neither properly diagnosed nor receive quality care, and will often face a long delay before they are diagnosed.

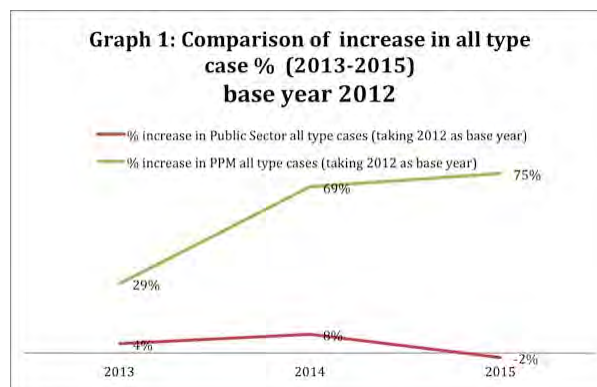
Public-private mix (PPM) is a crucial component for TB control. The majority of Pakistani population seeks healthcare in the private sector. Failure to involve the private providers results in delayed diagnosis, inappropriate and incomplete treatment and can contribute to drug resistance. Mercy Corps through the Global Fund support is implementing PPM in 75 districts. Between 2010 and 2015, we have diagnosed and registered 68,699 TB patients with treatment success rate of 93%, with participation of 3,178 private healthcare providers.

Intervention or response: Great emphasis was given on proper mapping and selection of private healthcare providers. A baseline KAP was done. All selected providers (GPs and labs) went through a specifically designed training program. The field-based staff (project and government TB staff) conducted robust coordination, monitoring and supervision, including EQA of laboratory diagnosis. Project is now providing small incentives to the GPs and lab staff. Contact tracing is done routinely, in addition to active case findings through mobile camps. We have recently introduced a mobile reporting pilot.

Results and lessons learnt: From 2011 to date, the project has seen a sharp and then steady increase in the number of cases reported by the participating providers. The public sector reporting over the same period has remained more or less stable (75% increase in PPM cases from 2012 baseline as opposed to negligible increase in public sector reporting). This shows that by investing in the PPM interventions, case reporting can be significantly increased.

Conclusions and key recommendations: Proper selection and training with certification is must. Active case finding using latest technologies, and simplifying data reporting are required. More investment needs to be done in PPM for better results.

Figure Increase in all types cases public sector vs PPM



OA-449-29 Study of impact of contact tracing of smear-positive TB cases on annualized TB notification rates in Maharashtra, India

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Background: Contact tracing of smear positive TB cases is recommended by WHO and is a guideline under National TB Control Programme. Though not uniformly implemented in country, Maharashtra State has implemented policy of contact tracing of smear positive TB cases. Hence this study was conducted in Maharashtra state for year 2015 in order to assess impact of policy of contact tracing of smear positive TB cases on annualized total case notification rates and pediatric case notification rates in India.

Methods: Cross sectional study was undertaken in all 79 RNTCP districts of Maharashtra. All RNTCP staff was trained in principles and Standard operating procedure for implementation of contact tracing. Prescribed formats for were utilized to capture data pertaining to contact tracing. Data was entered in analyzed in Excel. All smear positive TB cases registered in 2015 were included in the study.

Results: Contact tracing was done for 94% (60839 out of 64960) of smear positive TB patients. Average 3 adult contacts (182340 from 60839 patients) were identified for each smear positive TB patient. Out of adult contacts identified, 18% (33631) adults were presumptive TB patients. 1870 (6%) adult TB patients were diagnosed from presumptive TB patients who were tested. 0.70 Pediatric contacts were found for each smear positive case (42839 out of

64960 TB patients). 21% (8996 out of 42839) of the pediatric contacts were identified as presumptive TB cases. 955 (11%) pediatric TB cases were diagnosed from contact tracing. Contribution of adult contact tracing to total case notification of Maharashtra state was 1% in year 2015. Contribution of pediatric contact tracing to total pediatric case notification of Maharashtra is 14%. Overall contribution of contact tracing to total case notification is 2%.

Conclusions: Considering chain of transmission, Contact tracing remains an important tool in improving case notification. Contact tracing may result in early and improved case notifications for pediatric TB as well. Systematic implementation and routine capturing of data pertaining to contact tracing remains key to strengthen TB case notification through contact tracing. Extension of contact tracing activities to privately notified TB patients is highly recommended to National TB Programme.

OA-450-29 Differences in yield of active versus passive contact screening in urban DOTS-supported cities, Afghanistan

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Background: National guidelines recommend contact investigation for all bacteriologically confirmed pulmonary TB cases, but a passive strategy for TB contact management is used in Afghanistan. Challenge TB project implemented active contact screening July-December 2015 in four urban directly observed therapy, short course (DOTS) cities (Kabul, Herat, Kandahar and Jalalabad). This study compares results of active contact screening in intervention areas to passive contact screening in the control area.

Methodology: In the control area, only households of index cases were referred to health facilities, and most did not arrive. Intervention strategies included training healthcare workers, providing supportive supervision, collecting data and providing feedback, and contacting a random sample of 10% of TB index case contacts for cross check. All household contacts of bacteriologically confirmed TB cases (TB index cases) were visited in four provinces of Kabul, Kandahar, Herat and Nangarhar by health facility members. Contacts with cough for more than two weeks and sputum were taken to the nearest TB diagnostic center for sputum examination. All children under 5 were entered into the TB contact register and received IPT.

Results: During active contact screening in the intervention areas, 2,014 TB index cases were

registered and 10,183 household contacts were screened; among them, 303 (2.98%) TB cases were identified and 1,824 children under 5 were put on IPT. In the control area, 5,403 index TB cases were registered and 20,446 household contacts were screened. Among them, 290 (1.42%) were clinically diagnosed with TB, and 1,791 children under 5 received IPT. TB case yield among household contacts in the intervention and control areas was 2,976 and 1,418 per 100 000, respectively (Table).

Conclusion: TB among household contacts is eight times higher than WHO estimated incidence cases. Active screening almost tripled TB case detection and provision of IPT for children compared to passive contact screening. We recommend implementation of active contact screening nationwide.

Table Results in intervention and control area

	Index cases	Contacts of index TB cases	Clinically confirmed cases	Tests of significance
Intervention	2014	10 183	303	$P < 0.001$
Control	5403	20 446	290	

OA-451-29 Active TB case finding using contact investigation is a more efficient approach compared to targeted community TB screening outreach

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Background and challenges to implementation: Tuberculosis (TB) case finding in resource limited settings is predominantly 'passive' and reliant on the patient's initiative to seek health care services. TB case notification in Kampala has stagnated over the years. Track TB project supports the Kampala Capital City Authority to implement interventions to increase TB case finding in Kampala.

Intervention or response: From January to September 2015, community linkage facilitators conducted home-based symptom-based screening of close/household contacts of 3,820 index pulmonary bacteriologically confirmed TB patients. 242 community sensitization and TB screening outreaches were conducted in high TB burden parishes based on routine programme data. We compared the yield, number needed to screen (NNS) and number needed to test (NNT) between the two active TB case finding approaches using community and TB programme data.

Results and lessons learnt: Of 8,622 household

contacts screened, 2,256 were identified as presumptive TB patients; 1,067 of these were tested and 147 diagnosed with TB. Of the 14,016 individuals reached through targeted community outreach activities, 2,085 presumptive TB cases were identified and either referred or provided samples for laboratory testing; 63 clients were diagnosed with TB. The yield from contact investigation was 10 fold the WHO-estimated TB prevalence in the general population, compared the yield from targeted TB screening outreaches which is about 2.7 fold. The NNS for contact investigation and TB screening outreaches were 59 and 222 while the NNT for either approach were 7 and 33, respectively.

Conclusions and key recommendations: Active TB case finding through contact investigation is more efficient compared to community outreaches. We recommend increased investment in TB contact investigation as a key strategy for increasing TB case finding in similar urban settings.

OA-452-29 TB prevalence among individuals undergoing contact tracing and its determinants in Mandalay City, Myanmar

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Background: Globally, TB is still a public health problem in developing countries including Myanmar, one of 22 global highest TB-burden countries with prevalence, 473/100 000 population in 2013. Early detection and proper treatment of TB is key in controlling TB infection. Household contacts of infectious TB patients have high risk of becoming infected by TB and of developing active TB. Different countries performed various diagnosis procedures for contact tracing such as sputum smear, CXR or Xpert technology which detect TB differently. Although the contact tracing of TB is recommended worldwide, it has not been properly implemented particularly in resource-limited countries. In Myanmar, the policy of contact tracing is adopted but no routine data shows whether contact tracing was completely investigated or how many results were positive. The magnitude of the problem among TB contact tracing is crucial to put more effort on this policy.

Design and Methods: A cross-sectional study to assess the prevalence of TB and its determinants in household contact tracing was conducted in Mandalay City, Myanmar. The household contacts of TB patients who were under 3-month treatment were included regardless if they were children or adults. All contact tracing were visited by the research team for data collection who collected the sputum as well as

suggested health facilities nearby for CXR for all adults but only CXR were performed among children.

Results: A total of 174 contacts from 40 pulmonary TB random index patients were included. Of these contacts, 115 adults and 59 children were found. Of all contacts, positive TB was detected by CXR in 15.5% (27/174), from sputum smear in 5.1% (9/174) and by Xpert in 8.0% (14/174). Overall positive TB prevalence among contacts was 13%. Determinants of positive TB among contacts were low education, passive smoking, drinking, sharing room and care-taking by index TB patients. Additionally, no contacts cases could go to CXR centers by themselves, therefore, the researcher team organized their transportation.

Conclusions: TB prevalence among contacts was high, especially in children. Known risk factors were confirmed. The country needs to strengthen contact tracing process with support for transportation to get CXR.

OA-453-29 Tuberculosis among immigrant workers from highly endemic countries following pre-entry screening in Taiwan

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Background: Taiwan's criterion for admissions of new immigrant workers from tuberculosis (TB) highly endemic countries is a normal chest X-ray (CXR). All immigrant workers were mandatorily screened for TB, requiring of an approval of TB free by an overseas pre entry screening and by the post entry following-up screenings within 3 days as well as at 6th month, 18th month and 30rd month. This study aimed to estimate the TB incidence among these immigrant workers following pre-entry screening and to assess the effectiveness of post-entry mandatory TB screenings.

Methods: The TB prevalence was calculated by the Taiwan TB archive database, which was linked with a foreigner physical exam screening database.

Results: 2011-2014, 2,080 TB-positive cases were identified among 1,911,966 immigrant workers from South east Asia (Viet Nam: 16.0%, Indonesia: 48.1%, Philippines: 22.9%, Thailand: 12.0%) following their pre-entry screening and partial repatriating. Totally, the respective gender- and age (20-49 yrs)- specific TB incidence rate of 65.8-175.6 per 100 000/year was 2.1-5.5-fold greater than that of the corresponding Taiwanese individuals. In term of the diagnostics, 89.3% of all TB cases among immigrant workers were abnormal CXRs, 33.3% smear negative/culture positive and 15.9% smear positive/culture positive. Overall, these cases were comprised of 14.2% (298/2,080) smear-positive TB of high infectivity, 74.3% (1,544/2,080) smear- negative TB

of less infectivity and 7.8% (163/2,080) extra-pulmonary TB. In total, 58% of immigrant workers with TB were passively identified and 41% were actively identified via post-entry screenings; moreover, the former i.e., passively identified vs. actively screened TB cases had a higher proportion of smear-positive samples (189/1,223 vs. 108/857; odds ratio (OR) 1.56, 95% confidence interval (CI): 1.2-2.0). In terms of effectiveness, the TB yield of the mandatory screening at 6- 30 months post-entry was 61.1-180.5 cases per 100 000 screenings.

Conclusions: Immigrant workers from highly endemic countries remained a higher (2.2-2.5 fold) TB risk than domestic residents following pre-entry screening. These screening intervened to reduce the TB burden and resulted in a total of 74.3% smear-negative TB cases of less infectivity in an early pathogenesis. The proportion of pulmonary TB cases was significantly higher in illness identified ones than in actively screened ones (OR 1.56).

23. Interplay of tobacco control and broader health agenda

OA-459-29 With a little help from BAT: prices, bans and smoking onset in Chile

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Background: With one of the highest juvenile tobacco prevalence in the world, Chile has been implementing a number of initiatives to decrease tobacco consumption (graphic warnings, smoke-free policies, several bans to advertisement, smoking bans in public places, etc). More importantly, real tobacco prices have increased: between 2005 and 2013 they grew 87%. This increases were largely initiated by tobacco manufacturers and in particular by British American Tobacco (BAT) whose brands made up 92 to 98% of the Chile cigarette market.

Methods: We used data from seven waves of a nationally representative survey, conducted on school population. Such a survey covers the 2001-2013 period. We matched individual decisions (start/not start smoking) with observed real tobacco prices, since January 1980 to December 2013. We used discrete-time hazard models and a complementary loglog (cloglog) specification. As a functional form for the baseline hazard function, we used a cubic polynomial specification. As a sensitivity check, we also used a more flexible approach and used a dummy specification for time at risk, measured in years.

Results: All models suggest a large, negative and

statistically significant association between prices of tobacco products and the hazard of smoking onset. Price elasticity estimates fall within a fairly narrow range centred on -0.5. Including additional covariates does not alter price elasticity estimates in any significant or substantial way. The enactment of a law banning school smoking and selling close to schools decreased significantly onset hazard. Contrary to evidence found in other countries, women and higher SES individuals appear to be at higher risk of smoking onset than men and low SES individuals.

Conclusions: This study adds to the small but growing body of evidence from low- and middle-income countries that finds that higher tobacco prices decrease the hazard of smoking onset. The fact that price movements came largely from BAT pricing strategy does not decrease the effectiveness of price increases. Of particular interest is the finding that smoking bans in schools and restriction on selling points close to school have on onset in juvenile population.

OA-460-29 An analysis of major policy level intervention and tobacco epidemic trend in Madhya Pradesh, India

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Background and challenges to implementation: Government of India conducts National Family & Health Survey (NFHS) in order to know health and nutrition status in India. 4 rounds of NFHS conducted till now NFHS-3 conducted in 2005-06 and NFHS-4 conducted in 2015. In order to understand tobacco control intervention impact an analysis of major policy intervention and comparison of results of tobacco use and consumption in NFHS-3 and NFHS-4 was done.

Intervention or response: An analysis of major tobacco control policy intervention done in the field of tobacco control was done by using secondary data from governments websites, media and other relevant sources. Data related to tobacco consumption from NFHS-3 and NFHS-4 were analyzed for comparing trend of tobacco epidemic in Madhya Pradesh State of India.

Results and lessons learnt: Major policy level intervention were done by Government of Madhya Pradesh. Tax on tobacco products were increased during the period. Gutkha (mixture of areca nut and tobacco) banned in the state. Hookah bars in cities were banned. Health department in collaboration with civil society organized various training programs and awareness programs. State and district level tobacco control committee meetings were held. Enforcement strengthened, directives passed from state to district level. Comparing findings of National Health & Family Survey data of year 2005-06 and

2015-16 regarding tobacco use it was found out that: Women who used any kind of tobacco reduced from 16% to 10.4%, Men who used any kind of tobacco reduced from 68.5% to 59.5%. NFHS4 data of year 2015 showed that: Men who tried to stop smoking or using tobacco in any other form (during the past 12 months) was 37.2% and women who tried to stop smoking or using tobacco in any other form (during the past 12 months) was 38.5%.

Conclusions and key recommendations: Reduction in tobacco consumption and quitting rates shows that policy change in tobacco control can play an important role in reducing the burden of tobacco epidemic.

OA-461-29 Innovative health financing for tobacco control: the implementation and effectiveness of India's 'movie rules'

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Background: Tobacco consumption is a critical concern in populous low-income countries, like India. The social acceptability of tobacco perpetuates its use: the positive portrayal of tobacco in the media has been associated with increased consumption of tobacco. Hence, To counter the pro-tobacco imagery in the visual media, the Government of India modified its tobacco control law in 2011/2012 requiring film theaters and television channels to screen pre-approved anti-tobacco public service announcements and a disclaimer at the beginning and during the middle of programs when tobacco consumption is depicted and health warning scrolls on screen while tobacco is in use onscreen.

The 'Film Rule,' as this law amendment is known, has the potential for significant impact given the high viewership of such programming globally. It is also highly cost-effective since the onus of implementation lies on the broadcaster and not the government.

Method: Four studies were undertaken to monitor the genesis, implementation and effectiveness of the Rule. First, a news media analysis in the lead up the implementation of the Film Rule identified industry arguments against the Rule. Two observational studies, including exit interviews of cinema-goers, monitored the implementation and effectiveness of the Rule. Finally, legal research identified legal loopholes and opportunities.

Results: Findings from this comprehensive set of studies identified standard arguments against the Rule - such as impingement of creative freedom, arguments that health warnings are ineffective - and provide guidance for addressing these attacks preemptively. The observational studies identified over 80% compliance with the Film Rule in film theaters

but less than 10% compliance by television channels. Exit interviews among film-goers also found positive impact among those exposed to anti-tobacco messaging. Legal research identified strengths in the current law, enabling implementation, and opportunities for its advancement within existing media laws and procedures.

Conclusion: The Film Rule is a novel health financing mechanism for sustained mass media campaigns at low (or no) cost to governments. Our studies show positive impact of the Rule and offer valuable lessons for strengthening the law within India and for other countries considering similar approaches.

24. The Union student late-breaker session on lung health

OA-2666 Prevalence and molecular epidemiology of pulmonary tuberculosis at Hawassa prison center, Southern Region of Ethiopia

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Background: Control of tuberculosis (TB) in prisons is an important public health priority. In some settings, prisons have been recognized as reservoir and sites of transmission for TB. We sought to estimate the burden of TB in a large Ethiopian prison and assess the value of active case finding and transmission dynamics using molecular epidemiology.

Method: Active case-finding was carried out from June 2015 through January 2016 in a large prison upon informed consent. All prison inmates with cough of at least 2 weeks were investigated for TB. Two sputum samples (spot and morning) were collected from those with productive cough and examined using AFB smear microscopy, Xpert MTB/RIF test and culture. Isolates were tested for drug susceptibility (DST).

Results: A total of 2068 prisoners were screened of whom 385 (98%) were male, 250 (63%) originated from an urban area and their median age was 22 years (range 14-80 years). Five cases, kept separately from others, were found to be on treatment for TB. Only nine of 2040 screened (0.4%) were HIV-positive. Among 396 (19.1%) who had a positive cough screen, 8 (2%) tested positive for acid fast bacilli on sputum smear microscopy and 31 (8%) had a positive Xpert test. One case was confirmed as MDR-TB. The point prevalence of PTB was estimated to be 1748 per

100 000 persons. This rate of TB among incarcerated persons is ~16 fold higher than in the general population

Conclusions: A high prevalence of PTB was detected among persons incarcerated in Hawassa Prison in Ethiopia. Active case finding using a symptom screen in combination with Xpert can increase TB case detection and has the potential to interrupt transmission of *M. tuberculosis* in correctional facilities in high burden, low and middle income countries. The molecular epidemiologic data will provide information about transmission dynamics that would help in designing strategies to prevent TB in prisons.

OA-3024 MDR-TB patient support at outpatient stage of treatment in Ukraine

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Background: Ukraine has one of the lowest treatment success rates among MDR-TB patients in the EECA region, at 34.4% (cohort 2012, all TB cases). At the same time there is a high level of treatment interruption among MDR-TB patients - 14.9% (cohort 2012, all cases). Since 2013, Ukraine has been providing treatment for MDR-TB patients with second-line TB drugs procured with Global Fund funds. To improve treatment outcomes, the project 'MDR-TB patient support at outpatient stage of treatment' started in 2013.

Method: Those MDR-TB patients who received second-line TB drugs procured with GF funds were supported after their discharge from hospital by nurses of the Ukrainian Red Cross (RC). Nurses visited patients who were on out-patient stage of treatment every day and provided DOT (daily visits to control drug taking) as well as psychosocial support, management of side effects and food packages twice per month.

Results: Treatment outcomes for the 2013 patient cohorts were obtained in May 2016. To evaluate the influence of psychosocial support on treatment results two cohorts were analyzed: 1) patients who were treated with second-line TB drugs procured with GF funding and who received psychosocial support, and 2) patients who were treated with second-line TB drugs procured with GF funding and did not receive support. It was expected that psychosocial support of MDR-TB patients would impact on reducing the rate of treatment interruption and therefore improve treatment results. However, except for these indicators, we registered significant decreases in the failure of treatment and deaths among those patients who were supported by RC nurses.

Conclusions: MDR-TB patient support at outpatient stage of treatment is extremely important and can significantly improve treatment outcomes, which is

the sine qua non to achieve the goals of the Global End TB Strategy.

Table Comparison of treatment results in MDR-TB patients

	Patients who received RC support %	Patients who did not receive RC support %
Treatment success	85.9	44.4
Treatment interruption	3.0	18.2
Treatment failed	6.4	13.5
Died	1.3	12.5

OA-3036 Effectiveness of TB treatment regimens containing bedaquiline with repurposed drugs for drug-resistant tuberculosis in the Chechen Republic, Russian Federation

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Background: The prevalence of fluoroquinolone and/or injectable drug resistance is high amongst multi-drug-resistant tuberculosis (MDR-TB) patients in Chechnya. In June 2014, Médecins Sans Frontières (MSF), in collaboration with the Chechen Republican TB Dispensary, gained access to bedaquiline, clofazimine and linezolid for the treatment of patients with drug-resistant TB. We describe interim cohort outcomes for patients receiving bedaquiline with clofazimine and linezolid as part of a treatment regimen constructed according to WHO guidelines, and an association between their use and improved 6-month sputum culture conversion rates.

Method: Patients diagnosed with pulmonary MDR-TB resistant to fluoroquinolone and/or injectable drugs were included in this analysis. Those started on bedaquiline, clofazimine and linezolid as part of their treatment regimen were included in the intervention group, while patients recruited into the treatment programme prior to the availability of these drugs formed a control group. Six-month culture conversion rates are reported. Baseline characteristics and a survival time analysis (Kaplan Meier) are presented. Cox regression was used to estimate the association between bedaquiline use and 6-month culture conversion rates while adjusting for credible confounding variables.

Results: Eighty-eight patients fulfilled the inclusion criteria: 28 in the control group, 60 in the intervention group. Six HIV-positive patients were included. Both groups had similar demographic characteristics and baseline drug susceptibility tests. In the control group, 11/28 (39.3%) achieved sputum culture conversion after 6 months, compared to 34/49

(69.4%) in the intervention group. Median time to culture conversion was 117 days (range 38-178 days) and 63.5 days (range 5-155 days) in the control and intervention groups, respectively. In the multivariable Cox proportional hazards model, treatment with regimens containing bedaquiline, clofazimine and linezolid were associated with a faster time to culture conversion (aHR 2.61, 95%CI 1.23-5.53, $P=0.012$) compared to the control group. There was weak evidence suggesting an association between female gender and faster time to culture conversion (aHR 1.72, 95%CI 0.93-3.20, $P=0.08$).

Conclusions: Our preliminary results suggest that regimens containing bedaquiline, clofazimine and linezolid led to higher rates of culture conversion by 6 months and reduced time to culture conversion when compared to regimens not containing these drugs.

OA-3075 Lansoprazole use and tuberculosis disease, a primary care based cohort study

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Background: An in vitro screen for compounds with activity against *Mycobacterium tuberculosis* previously demonstrated that the proton pump inhibitor (PPI) lansoprazole is highly active against both drug sensitive and resistant strains. Other PPIs, omeprazole and pantoprazole, are not. We estimated hazard ratios (HR) for incident tuberculosis disease (TB) in adults prescribed lansoprazole compared with adults prescribed omeprazole or pantoprazole.

Method: We used an extract from the Clinical Practice Research Datalink primary care database - routinely captured electronic healthcare records from the UK. The outcome was first recorded TB disease. New PPI users were identified and subsequent time divided into periods of exposure to 1) lansoprazole, 2) omeprazole or pantoprazole, or 3) no PPI. A Cox model compared the hazard of TB amongst lansoprazole users with omeprazole or pantoprazole users. Adjustment was made for numerous potential confounding variables. It has previously been estimated that the median time from TB infection to onset of symptoms is 1.26 years, therefore in the primary analysis, we assumed disease onset occurred 12 months before presentation. We varied this period from 0 to 5 years in sensitivity analyses. As a negative control, we repeated the analysis with myocardial infarction as the outcome.

Results: We identified 528,438 lansoprazole and 925,142 omeprazole or pantoprazole users. Their

median age was 55 years, 55% were female. A comparison of person-time on lansoprazole and person-time on pantoprazole or omeprazole yielded an adjusted HR for TB disease of 0.67 (95% CI 0.52-0.85). Comparing past users of lansoprazole and past users of pantoprazole or omeprazole, the adjusted HR for TB disease was 0.94 (0.75-1.17). Results were similar in sensitivity analyses. The adjusted HR for the negative control outcome of myocardial infarction comparing current users of lansoprazole against current users of pantoprazole or omeprazole was 1.01 (0.98-1.05).

Conclusions: Current use of lansoprazole was associated with reduced risk of TB disease. Lansoprazole's in vitro activity against *M. tuberculosis* may be clinically relevant. Given its favourable side effect profile, lansoprazole (or lansoprazole sulphide, the metabolite thought responsible for anti-*M. tuberculosis* activity) may prove a useful addition to regimens for the treatment of latent infection or TB disease.

OA-3116 Establishment of interpretive criteria for phenotypic bedaquiline resistance determination and association with clofazimine resistance

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Background: Bedaquiline (BDQ) is a novel agent approved for the management of M/XDR TB treatment. South Africa (SA) has embarked on a large scale roll out of bedaquiline and monitoring resistance is critical to protect this new agent. Criteria for determination of resistance are poorly established but are recommended as part of country implementation. We sought to determine epidemiological cut-offs (ECOFFs) for BDQ on microbroth, agar and MGIT 960. Cross resistance to clofazimine (CFZ) and this was examined.

Method: All available rifampicin resistant, a selection of fully susceptible and mono resistant TB strains from the recent national drug resistance survey in SA were used. Strains were tested against a serial dilution of bedaquiline minimum inhibitory concentrations (MICs) on 7h9 microbroth dilution (ThermoFischer), 7h11 agar and MGIT-960 (Becton-Dickinson). Additionally whole genome sequencing (WGS) was performed on all strains using the MiSeq platform (Illumina). Validation of the ECOFF was determined using error rate bounded method as defined in the CLSI M23-A3 guidelines. Frequency distributions were plotted against putative resistance genes and MIC. Cross tabulation of MICs defining BDQ and CFZ resistance was performed.

Results: A total of 400 strains distributed across all 9 provinces were tested and MICs determined in 395, 396 and 400 for the broth, agar and MGIT methods. The ECOFF determined was 0.25ug/ml, 1ug/ml and 2ug/ml respectively. The ECOFF for MGIT is shown in Figure 1 (not shown). The very major errors were 0.8% for both agar and MGIT while the major errors were 2.0% and 1.5%, respectively. These were within the bounds defined by CLSI (< 1.5% and 3.0%). No *atpE* mutations were detected while mutations in *Rv0678*, *PepQ* and *Rv 1979* were not associated with BDQ resistance. Cross resistance between CFZ and BDQ is shown in Figure 2 (not shown). Four of the 6 isolates resistant to CFZ were also resistant to BDQ while 4 of 5 isolates resistant to BDQ were also resistant to CFZ. These were predominantly in XDR cases.

Conclusion: ECOFFs have been established for determination of bedaquiline resistance and putative mutations were not associated with resistance. Clofazimine cross-resistance was observed but primarily observed in XDR cases.

OA-3125 Application of the shorter MDR-TB regimen in high M/XDR-TB burden prison system of Azerbaijan

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Background: In May 2016, the World Health Organization (WHO) recommended the use of standardized shorter multidrug-resistant (MDR) tuberculosis (TB) treatment regimen for patients with rifampicin resistant (RR) TB, including MDR-TB, which is deemed to be less toxic, more effective in terms of patients' compliance and cost-effective for the TB programmes. In 2015, the proportion of MDR-TB patients in the Penitentiary System (PS) of Azerbaijan was as high as 7% among newly treated and 24% among previously treated TB patients. However, it is unknown, what proportion of patients fulfils the criteria of allocation to the shorter-course treatment.

Objective: To estimate the proportion of RR-TB including MDR-TB patients, who may benefit from the newly recommended regimen in high MDR-TB burden settings of the PS of Azerbaijan.

Method: We assessed all cases notified in Azerbaijan PS during the period 01.01.2011-31.12.2015 and estimated the proportion of those, who would have met the eligibility criteria for the shorter MDR-TB regimen, i.e. new pulmonary RR-TB, including

MDR-TB cases sensitive to fluoroquinolones, second-line injectables and pyrazinamide.

Results: Overall 2463 TB cases including 378 RR-TB (15.3%) and 375 MDR-TB (15.2%) cases were notified in the PS during the study period. Out of RR-TB - 19.6% and out of MDR-TB cases - 18.8% met the eligibility criteria for the shorter MDR-TB regimen (Table).

Conclusions: Our analysis shows that in high MDR-TB burden settings, like PS of Azerbaijan, about one fifth of registered RR-TB, including MDR-TB cases may benefit from the 2016 WHO recommended shorter MDR-TB regimen. However, the proportion is too small when applied to overall notified TB patients.

Table. The proportion of cases of rifampicin resistant and multidrug-resistant tuberculosis registered in Penitentiary System of Azerbaijan, 01.01.2011-31.12.2015 eligible to be treated according to the WHO-recommended shorter regimen.

	MDR-TB cases eligible for WHO-recommended shorter MDR-TB regimen (%)	RR-TB cases eligible for WHO-recommended shorter MDR-TB regimen (%)	All RR-TB cases
2011	26 (23.4)	26 (23.4)	111
2012	20 (19.2)	20 (19.2)	104
2013	14 (18.7)	14 (19.7)	71
2014	6 (11.5)	9 (17.3)	52
2015	5 (12.5)	5 (12.5)	40
Total	71 (18.8)	74 (19.6)	378

FQ= fluoroquinolones; MDR=multi drug resistant; RR=rifampicin resistant; TB=tuberculosis; WHO=World Health Organization; Z=pyrazinamide.

OA-3138 Short-course regimen for MDR-TB in a high HIV prevalence setting: model of care in Swaziland

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Background: In May 2016 WHO updated the recommendations on treatment of multidrug-resistant tuberculosis (MDR-TB) supporting the use of a shorter MDR-TB treatment regimen. Médecins sans Frontières (MSF), with the Swaziland Ministry of Health, has been using the short-course regimen (SCR) in Swaziland in two sites since January 2014. We present model of care and interim results.

Methods: From January 2014 to June 2016 we started SCR on 129 new presumptively MDR-TB patients diagnosed with Xpert® MTB/RIF or confirmed from culture and drug sensitivity test. The model of care developed by MSF relies on a caregiver team composed of 1 MD, 1 nurse, 1 counsellor, 1 outreach team. The treatment is administered and observed daily by a treatment supporter. All patients with severe clinical conditions are hospitalized. Patients undergo treatment follow-up at 2 weeks after MDR-TB treatment initiation followed by monthly follow-up until treatment completion. Treatment monitoring integrated ECG monitoring, audiometry and laboratory tests. Psychosocial support is part of the package of care: weekly support group,

adherence counselling and monthly home visits. Socio-economic incentives are provided including transport allowance for patients and treatment supporters, monthly fee for treatment supporter and monthly food packages for patients.

Results: Under this model of care 80 patients (79% HIV+) completed treatment between Jan 2014 to June 2015 achieving a 75% success rate ($n=60$). 10 patients died (12.5%), 9 failed (11.3%) and 1 (1.3%) patient was lost to follow-up (LTFU). Culture conversion at 4 months of treatment was 67%. Severe adverse events grade 3 and 4 occurred in 30 (23.3%). At 4 weeks median QTc increase was 34 ms.

Conclusions: A model of care including psychosocial support and enablers for the short-course regimen led to satisfactory culture conversion and interim outcomes of MDR-TB treatment in high HIV co-infection setting.

Table Description of activities

	1st visit	In between	Initiation	Monthly monitoring
MD	History & physical examination		Assessment of nutrition status Interpretation of baseline tests results Plan/treatment for concomitant diseases Treatment initiation	Physical examination AE check Interpretation of lab tests
Nurse	ECG Audiometry Schedule CXR	Arrangement daily injections		Audiometry (IP) ECG request Lab tests
Psychosocial and outreach team	Counselling	Identify treatment supporter Assessment: Home IC Socio-economic	Counselling Assessment Treatment supp.	Adherence counselling Monthly home visits: DOT assessment & patient
Examinations	Blood extraction Sputum culture/DST	CXR		Monthly tests (blood, sputum)

OA-3141 Effectiveness of isoniazid preventive therapy to prevent tuberculosis among people living with HIV in KwaZulu-Natal, South Africa: a cohort study

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Background: According to the World Health Organization, tuberculosis (TB) preventive therapy is a pivotal tool to achieve the 90-90-90 targets. Isoniazid preventive therapy (IPT) is the currently recommended TB prophylaxis in countries with a high burden of TB-HIV. The recent implementation of IPT in these

settings overlapped with the broader roll out of antiretrovirals among people living with HIV (PLWH), making it difficult to differentiate the effectiveness of IPT to prevent TB disease in this population. Since 2011, 6-month IPT has been offered to PLWH in uMgungundlovu District, Kwa-Zulu-Natal. We sought to determine the effectiveness of IPT among PLWH on antiretrovirals in this high-burden setting.

Methods: We conducted a retrospective cohort study of PLWH on antiretrovirals who initiated on IPT between 2011-2012 in a large community health centre catchment in uMgungundlovu. We defined IPT-users as individuals who collected ≥ 5 months of IPT compared to never-users. IPT-users ($n=63$) were frequency matched to non-users ($n=7514$) by month and year of ARV initiation. We defined a case as any active TB confirmed by smear, culture, or GeneXpert during IPT-use or 18 months of follow-up. Given a zero cell for exposed cases, we used a generalized linear model (GLM) to estimate risk difference (RD), including the frequency group variable in the model to account for matching. Additionally, we considered baseline CD4 count, age, and antiretroviral regimen in the model.

Results: Zero cases of TB arose among the 63 IPT-completers, while 292 cases of confirmed TB developed amongst never-users. Results from GLM analysis suggest that after controlling for CD4 cell counts below 250, the risk of TB among PLWH on antiretrovirals is 2 per 100 over a 2-year period ($P < 0.001$), a risk that diminishes to nil if 6-month IPT is taken to completion ($RD = -0.035$, $P = 0.14$, CIRD $-0.08-0.01$). Although error estimates are less reliable with the use of GLM for binary data, risk differences in stratified cohort analysis were significant, suggesting the trend holds.

Conclusions: Amongst PLWH on antiretrovirals in a high-burden TB-HIV district of South Africa, 6-month IPT appeared to markedly reduce the risk of TB over a 2-year period compared to never-users.

OA-3143 Operational research: delays of treatment initiation in first time diagnosed TB patients in Ukraine from health care system prospective

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Background: Ukraine is among the world's 27 high-MDR-TB burden countries: 22% of new cases and 56% of previously treated patients are MDR-TB cases. The overall treatment success rate in Ukraine is only 69.6%, including 38.4% among MDRTB cases.

Previous research results suggests that treatment initiation delays seriously jeopardize the outcomes.

Design/Methods: In 2015 USAID's Strengthening Tuberculosis Control in Ukraine project awarded a grant to a team of MPH student researchers from the School of Public Health of the National University of 'Kyiv-Mohyla Academy. From October 2015 to June month 2016, the team conducted operational research to identify the average duration of TB treatment initiation and the variables that are associated with the delay. This operational study has a mixed design and combines retrospective cohort analysis of 41 733 patients first diagnosed with TB in 2014 and qualitative content analysis of 33 interviews with medical staff involved in TB diagnostics and care in 5 oblasts (regions) of Ukraine with both high and low TB burdens.

Results: On average, the treatment initiation time was 25 days from accessing health care. Regions varied from 13 days in Zhytomyr region to 47 in Vinnitsia region with no association with regional TB burden. After adjusting covariates, the following variables were found to increase the average treatment initiation time: age under 18 (44 days), extrapulmonary TB (40 days), urban habitation (28 days), female (28 days), and history of imprisonment (36 days). The qualitative approach revealed the following barriers for timely treatment initiation: geographical disconnection, conflicting time schedules, poor laboratory capacities at first-level health care facilities (including shortfall of technologies, procedures, and experienced personnel). Motivation of patients to start TB treatment is influenced by stigma towards people with TB in the general population and among health professionals.

Conclusion: Referral from first-level facilities to TB care and laboratory capacities on both levels should be strengthened to avoid delays in TB treatment initiation. Diagnostic algorithms for extrapulmonary and pediatric TB need improvement. Reducing stigma within the health care system and among general population is another important direction of shortening the treatment initiation time.

25. Childhood TB, MDR and pharmacokinetics

OA-462-29 Long-term safety, tolerability, and pharmacokinetics of delamanid in children aged 7-11 with MDR-TB

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Background: MDR-TB treatment in children is long and toxic; safer and better tolerated drugs are urgently needed. Delamanid, a nitroimidazooxazole anti-TB agent, has demonstrated efficacy in adult clinical trials of MDR-TB. The aim of this study was to assess long-term safety, tolerability, and PK of delamanid in younger children with MDR-TB.

Methods: A Phase 2, open-label, uncontrolled, trial of delamanid in children with MDR-TB was performed in the Philippines and South Africa (NCT01859923). Delamanid 50mg po BID was administered with an optimized background regimen (OBR) for 6 months followed by OBR alone per WHO guidance. Safety was assessed every 2-4 weeks up to one year. PK sampling for concentrations of delamanid and DM-6705 (a key metabolite) was performed intermittently between days 1-238.

Results: 6 patients were enrolled (4 Philippines; 2 South Africa). 3 had confirmed and 3 presumptive MDR-TB. The median age=9.5 years (range:7-11); 2 were male; the median weight=25kg (range:16-34). No patient discontinued trial participation. The most common adverse events were headache and upper respiratory infection (3 patients for each). No patient experienced a QTcF >500ms or change from baseline of >60ms. Median delamanid concentrations=356-454ng/mL (within adult range). Median DM-6705 levels=103-173ng/mL (lower than adults after week 8).

Conclusions: Long-term exposure to delamanid 50 mg BID was well-tolerated in this cohort. Delamanid concentrations were within the range seen in adult clinical trials, suggesting that 50mg BID is adequate for this age and weight group. Additional trials are underway to assess the safety and PK in younger aged children.

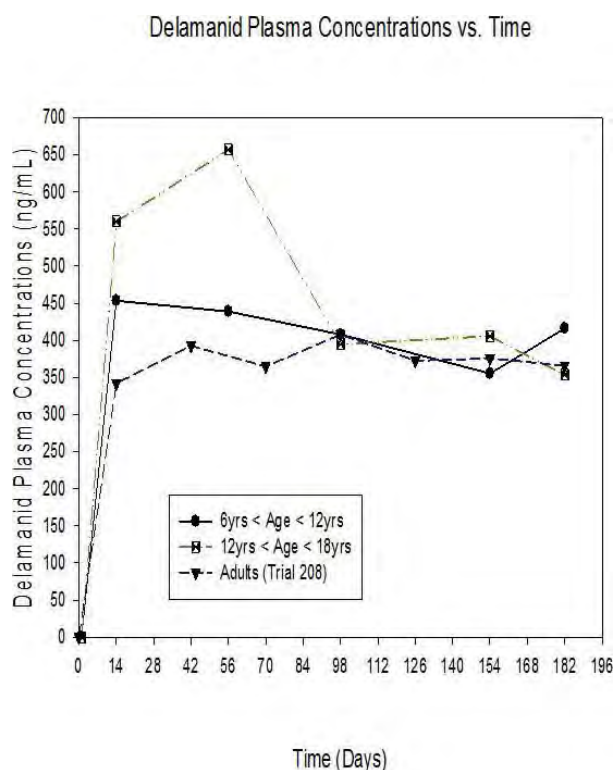


Figure Delamanid plasma concentrations]

OA-463-29 Effect of co-administration of lignocaine on pain and pharmacokinetics of intramuscular amikacin in children with multidrug-resistant tuberculosis

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Background: Current treatment regimens for multidrug-resistant (MDR) tuberculosis (TB) are recommended to include at least 6 months of an injectable medication. These are painful and poorly tolerated. The objective of this study was to evaluate the impact of co-administering lignocaine on pain and pharmacokinetics of intramuscular injections of amikacin in children.

Methods: Children 8-18 years routinely receiving amikacin for MDR-TB treatment in Cape Town, South Africa, were eligible for this randomized blinded crossover trial. Each participant received an injection with and without additional lignocaine on different days, and was randomized to sequence. On the assessment days, an exact 20mg/kg dose of amikacin was prepared, with or without lignocaine. Plasma samples were drawn pre-dose, and then 1, 2,

4, 6 and 8 hours post-dose. Pain was assessed by participants using the validated Wong Baker FACES pain scale (0 to 5) pre-dose, then immediately, at 30 and 60 minutes post-injection. Participants and staff completing evaluations were blinded to sequence.

Results: Twelve children were included, median age 11.5 years (IQR 9.9-13.4y); 8 (67%) were male, 3 (25%) were HIV-infected, 4 (33%) were underweight for age. The median area under the concentration time curve (AUC)₀₋₈ of amikacin was 109.0µg*h/mL (IQR 84.7-121.3) with lignocaine compared to 103.3µg*h/mL (IQR 81.7-135.0) without lignocaine ($P=0.814$). The median maximum plasma concentration (C_{max}) was 36.7µg/mL (IQR 34.1-40.5) with lignocaine compared to 34.1µg/mL (IQR 35.6-46.4) without lignocaine ($P=0.638$). Participant-reported pain scores immediately after the intramuscular amikacin injection were significantly lower when lignocaine was co-administered: 1.0 (IQR 0.5-2.0) with lignocaine vs. 2.5 (1.0-4.0) without lignocaine ($P=0.004$). Pain scores after 30 minutes were 0.0 (IQR -0.5 to 0.5) with lignocaine, vs. 1.0 (IQR 0.0-1.5) without lignocaine ($P=0.107$) and after 60 minutes were 0.0 (IQR -1.0 to 0.5) with lignocaine vs 1.0 (IQR 0.0-1.0) without lignocaine ($P=0.075$).

Conclusions: The co-administration of lignocaine with intramuscular injections of amikacin did not significantly alter amikacin AUC or C_{max} , and resulted in significantly reduced pain immediately after the injection. TB programmes should routinely co-administer lignocaine with injectable TB medications to improve their tolerability in children.

OA-464-29 Population pharmacokinetics of levofloxacin in HIV-infected and -uninfected children with multidrug-resistant tuberculosis

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Background: Levofloxacin is increasingly used for treatment and prevention of multidrug-resistant (MDR) tuberculosis (TB). However, there are limited paediatric pharmacokinetic data, and paediatric doses required to achieve target exposures in adults are unclear.

Methods: This intensive pharmacokinetic study enrolled children 0-14 years routinely receiving levofloxacin for MDR-TB treatment or prevention in Cape Town, South Africa. After ≥ 2 weeks of treatment, children underwent sampling following an exact 15 or 20 mg/kg levofloxacin dose, given as

whole tablet (s) or crushed, orally or by nasogastric tube. Samples were collected pre-dose and at 1, 2, 4, 6, and 8 hours post-dose. Pharmacokinetic parameters were calculated using non-linear mixed effects modelling (NONMEM 7.3 with FOCE-I). The effect of body size was captured with allometric scaling; the effects of age, HIV status, treatment indication and administration method were evaluated in the model. Simulations from the final model were used to estimate doses across weight bands, targeting adult exposures using 500mg, 750mg, and 1000mg doses. **Results:** 109 children were included, median age 2.1y (range 0.3-8.7y) and weight 12kg (range 6-22kg). Levofloxacin followed 2-compartment kinetics with 1st-order elimination and absorption through transit compartments. After inclusion of allometric scaling, which substantially improved fit, the model characterised age-driven maturation of clearance (CL) with an effect reaching 50% around 2 months after birth. CL in a 12kg, 2-year-old child was estimated at 4.7 L/h. Nasogastric tube use increased the absorption rate, but did not affect bioavailability. HIV infection was associated with 16% slower CL. Levofloxacin exposures were substantially lower than reported in adults receiving a similar mg/kg dose (1000 mg): 45 vs. 129 mg·h/L, which was only partly explained by allometric scaling. To achieve exposures similar to adults higher levofloxacin doses than those currently recommended are required, particularly in smaller children with up to 50 mg/kg needed to approximate the 1000mg adult dose in some weight-bands.

Conclusions: Children achieve levofloxacin exposures considerably lower than adults using the same mg/kg dose. Paediatric doses likely to achieve target exposures in adults are substantially higher than currently recommended; optimal and safe levofloxacin dosing in children with and without HIV needs further investigation

OA-465-29 Baseline predictors of multidrug-resistant tuberculosis treatment outcomes in children: a retrospective cohort study

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Background: Globally, over 30,000 children fall sick with multidrug-resistant tuberculosis (MDR-TB) every year. Without robust pediatric data, clinical management follows international guidelines based on studies in adults and expert opinion. We aimed to identify baseline predictors of death, treatment

failure, and treatment default among children with MDR-TB disease treated with second-line drugs.

Methods: This retrospective cohort study included all children ≤ 15 years old with confirmed and probable MDR-TB disease who began tailored regimens in Lima, Peru between 2005 and 2009. Using logistic regression, we examined associations between patient and treatment characteristics and (1) death and treatment failure and (2) treatment default.

Results: 211 of 232 (90.9%) children had known treatment outcomes, of which 163 (77.2%) achieved cure or probable cure, 29 (13.7%) did not complete treatment, ten (4.7%) experienced treatment failure, and nine (4.3%) died. Independent baseline predictors of death or treatment failure were the presence of severe disease (aOR 4.96, 95%CI 1.61–15.26) and undernutrition (aOR 3.39, 95%CI 1.20–9.54). We did not identify any independent predictors of treatment default.

Conclusions: High cure rates can be achieved in children with MDR-TB using tailored regimens containing second-line drugs. However, children faced significantly higher risk of death or treatment failure if they had severe disease or were undernourished. These findings highlight the need for early interventions that can further improve outcomes for children with MDR-TB.

OA-466-29 The impact of household environmental tobacco smoke exposure on risk of TB infection in children with household TB exposure

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Background: Reducing TB transmission in households is an important strategy to prevent TB infection and disease in children. There is strong evidence linking environmental tobacco smoke (ETS) exposure and TB infection and disease in adults, but evidence in children is limited. We investigated the association between household ETS exposure and prevalent *Mycobacterium tuberculosis* infection in children with household TB exposure.

Methods: Children (3 months-15 years) with recent household adult pulmonary TB exposure were recruited from three community clinics in Cape Town, South Africa. Data were collected through structured caregiver interviews, clinical and laboratory evaluations at enrolment and month 3. *M. tuberculosis* infection was defined as either positive

tuberculin skin test (TST; ≥ 10 mm HIV-uninfected/ ≥ 5 mm HIV-infected) or positive interferon gamma release assay (IGRA; either T-SPOT.TB/Quantiferon-TB Gold-in-Tube) as per manufacturer's guidelines (baseline or month 3). Univariate and multivariate analyses (random effects logistic regression adjusting for household clustering) were completed, including age, previous TB and TB contact score as a priori confounders.

Results: 671 child TB contacts [median age 5.3 years (IQR 2.8-9.0)], 357 (53.2%) female; 539 (80.7%) mixed race ethnicity) were enrolled. Three quarters (513/76.5%) had reported household ETS exposure. TB infection was prevalent in 342/665 (51.4%) and 378/663 (57.0%) contacts by TST and IGRAs respectively. Odds of TB infection were three times higher in child TB contacts exposed to household ETS after adjusting for age, previous TB, TB contact score, housing type and structure and cellular telephone access (TST aOR 3.26, 95%CI 1.67-6.33, $P=0.001$; IGRA aOR 3.12 (95%CI 1.52-6.39, $P=0.002$)). A dose-response was observed in multivariate analyses, with odds of *M. tuberculosis* infection increasing 1.6 times for every additional two household smokers reported (TST aOR 1.62 (95%CI 1.18-2.23, $P=0.003$; IGRA aOR 1.57 (95%CI 1.10-2.24, $P=0.013$)). The population attributable fraction (PAF) of smoking for *M. tuberculosis* infection amongst child TB contacts using the more conservative IGRA-based estimate was 0.56.

Conclusions: In this high-burden TB setting, we found frequent ETS exposure in children with household TB exposure. The high PAF emphasizes the potential impact that smoking cessation interventions could have to reduce *M. tuberculosis* infection amongst child TB contacts in settings where both TB and tobacco usage are highly prevalent.

OA-467-29 Characteristics and outcomes of early versus late ART initiation in HIV-infected, ART-naïve children diagnosed with TB disease in Mbeya, Tanzania

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Background: In ART-naïve HIV-infected children with TB, the optimal timing ART initiation following antituberculosis treatment (ATT) initiation is unknown. This study aims to measure associations between clinical outcomes of ART naïve HIV-infected children and timing of their ART initiation following ATT.

Methods: Retrospective chart review March 2013 to

December 2015 of ART naïve children at the Baylor College of Medicine Children's Foundation - Tanzania clinic in Mbeya, Tanzania. 'Early ART' group initiated ART 0-14 days after ATT; 'Late ART' group initiated ART 15 days or more after ATT. The baseline and outcomes data of the two groups were compared using χ^2 or Fisher's exact test for categorical measures and Wilcoxon rank-sum test for age.

Results: 47 ART naïve patients with TB started ART, with 22 (47%) Early ART and 25 (53%) Late ART. Baseline characteristics did not differ between the groups other than Late ART group being older (Table A). Both groups showed high rates of severe/advanced immunosuppression, severe/moderate acute malnutrition, and low rates of bacteriologically-confirmed TB. The majority of ART naïve patients had favourable outcomes, regardless of ART timing; these outcomes did not differ between the two groups (Table B). TB-IRIS was not reported in any patients.

Conclusions: Both Early ART and Late ART groups showed good rates of favourable outcomes with no differences between the group. These findings demonstrate that initiation of ART - even as early as within 2 weeks of ATT - in ART naïve children lead to favourable outcomes, and delayed ART initiation is not necessary to achieve good clinical outcomes.

Table A) Comparison of baseline characteristics between 'Early' and 'Late' ART groups

Characteristic	Early ART (n=22)	Late ART (n=25)	P value
Age (median, range)	5.1 (1.6-8.9)	8.7 (4.8-12.1)	0.04
WHO suppression: - severe/advanced (%) [n=19]	10 (52.6)	12 (54.6)	0.90
Nutritional status: -SAM/MAM (%)	15 (68.2)	19 (76.0)	0.55
Diagnostic certainty: - confirmed TB (%)	3 (13.6)	5 (20.0)	0.51

B) Comparison of TB, nutritional and immunosuppression outcomes

Clinical Outcomes at 6 months	Early ART group with favourable outcome n (%)	Late ART group with favourable outcome n (%)	P value
TB outcome of 'completed treatment of cure'	15 (71.4%) [N=21]	20 (83.3%) [N=24]	0.48
Nutritional outcome of 'Not SAM'	14 (93.3%) [N=15]	20 (100%) [N=20]	0.43
Immunosuppression outcome of 'mild or not significant'	12 (85.7%) [N=14]	12 (70.6%) [N=17]	0.41

OA-468-29 Risk factors for complications and poor treatment outcomes in children with tuberculosis in Spain

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Background: Children have increased risk of tuberculosis (TB) dissemination and disease severity, and contribute critically on overall TB-associated morbidity and long term sequelae. We aim to describe the risk factors for complications and poor treatment outcomes of pediatric TB cases in Spain.

Methods: We analyzed childhood TB cases enrolled prospectively in the nationwide, multi-center Spanish Pediatric TB Research Network (pTBred). We assessed the incidence of acute complications at diagnosis, complications during antiTB treatment (including paradoxical reactions), and site-specific long-term sequelae. Ethical approval from all the participant centers was obtained. We calculated associated risk factors with multivariable logistic regression models.

Results: Between 2014 and 2015, 340 children with TB were enrolled (50% males; median [IQR] age 5.3[2.9-11.4] years). Of them, 34.4% were confirmed TB cases. Overall, the prevalence of complications was 16.7% (8.6% at diagnosis, 10.2% during treatment, including 6 children with both), and 4.1% of the children developed long term sequelae. Two children died of TB. Complications were more frequent in children < 1 year (54.5%, $P < 0.0001$), in those born to foreign parents (24%, $P = 0.002$), miliary TB (71.4%, $P = 0.002$), TB meningitis

(63.6%, $P < 0.0001$), and skeletal TB (100%, $P = 0.004$). In multivariate analysis, complications were associated with age < 1 year (OR 4.8[1.7-13.9], $P = 0.003$), TST induration < 5mm (OR 3.1[1.9-7.4], $P = 0.04$), bacteriological confirmation (OR 3.3[1.5-7.4], $P = 0.003$) and TB meningitis (OR 4.2[1-18], $P = 0.04$). Long-term sequelae were associated with miliary TB (OR 18[2.1-163], $P = 0.008$) and TB meningitis (OR 15.1[2.7-83.7], $P = 0.002$).

Conclusions: In Spain, one sixth of pediatric TB cases develops complications, which are strongly associated with early infancy, extrapulmonary disease and enhanced bacteriological confirmation. In our low-burden country, miliary and meningeal TB are still responsible of significant long-term sequelae and permanent disabilities

Table Characteristics of children with TB complications

	Complications (41/245)			Sequelae n=14/219		
	No	Yes	p	No	Yes	p
Demographics						
Male	51.5	51.2	.8	50.7	42.9	.5
<1 yr	5	29.3	<.001	6.4	21.4	.07
1-5 yr	39.6	31.7	.3	40.7	21.4	.8
5-10 yr	32.2	14.6	.02	30.4	21.4	.7
>10 yr	23.3	24.4	.8	22.5	35.7	.3
Nationality						
Foreign child	14.2	22	.2	16.6	14.3	.8
Foreign mother	46.8	73.2	.002	48	85.7	.006
Foreign father	45.5	65	.02	45.5	71.4	.06
Immune suppression	2.9	2.4	.1	2.9	0	.5
Clinical presentation						
Fever	28.7	65.9	<.001	39.5	57.1	.1
Loss of weight	10.6	36.8	<.001	13.6	15.4	.8
Asthenia	14.9	45	<.001	17.8	42.9	.03
Cough	46.3	58.5	.1	46.8	57.1	.4
Respiratory distress	8.4	16.8	.001	8.3	21.4	.1
Letargy	3	9.8	.06	3.9	14.3	.07
Diagnosis						
TST <5mm	5	22.5	.001	5	14.3	.1
TB confirmation	33.9	81.8	<.001	30	57.1	.07
Drug resistance	1.8	0	.4	1.7	0	.8
Site of TB						
EPTB	13.3	34.1	<.001	12.3	50	.001
EPTB + Pulmonary TB	40.7	84.6	<.001	44	85.7	.08
Lymphatic TB	7.86	9.8	.7	6.3	14.3	.2
TB Meningitis	2	17.1	<.001	2	28.6	.001
Skeletal TB	0	7.3	.004	0	14.3	.004
Miliary TB	1	12.2	.002	1	21.4	.002
Abdominal TB	0.9	9.1	.166	1.5	0	.1
Index case						
Not identified	31.9	45	.1	67.8	42.9	.07
Foreign index case	44.6	65.7	.02	44.6	71.4	.04

OA-469-29 Contribution of global tuberculosis to the burden of pediatric TB in the United States, 2007-2014

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Background: Characterizing the contribution of global TB to the burden of TB among children in the United States might inform improved prevention strategies.

Short abstract session, Saturday, 29 October

Methods: We analyzed data for children aged < 15 years reported to the National Tuberculosis Surveillance System (NTSS) in the 50 U.S. States, District of Columbia and Puerto Rico during 2007-2014. Parental nativity was available in NTSS for 2010-2014. We calculated TB incidence rates using population denominators from the U.S. Census Bureau.

Results: Of 4,767 children with TB reported during 2007-2014, 1,131 (24%) were foreign-born. Overall, the rate of TB among children in the United States was 1.0 per 100 000 person-years (95% confidence interval [CI]: 0.9, 1.0); however, the rate was >10 times as high (rate ratio 10.1; 95%CI : 9.4, 10.8) in foreign-born children compared to U.S.-born children—8.1 vs. 0.8 per 100 000 person-years, respectively. Among U.S.-born children during 2010-2014, 62% ($n=1,223$ of 1,987) had at least one foreign-born parent. For U.S. born children for whom the nativity of both parents was known, the rate of TB was 3.7 (95%CI : 3.1, 4.4) and 8.7 (95%CI : 7.7, 9.8) times as high among children with one and two foreign-born parents, respectively, compared to children with two U.S.-born parents. Overall, 70% ($n=1,815$ of 2,579 from 2010-2014) of children with TB had foreign birth ($n=592$) or were U.S.-born with at least one foreign-born parent ($n=1,223$). Among foreign-born children with dates of U.S. entry available reported during 2007-2014 ($n=1,058$), 62% ($n=659$) were diagnosed with TB within one year of U.S. entry (Figure 1).

Conclusions: The global TB epidemic plays a large role in the epidemiology of TB among children in the United States. The high proportion of foreign-born children diagnosed with TB soon after U.S. entry highlights the importance of pre- and post-immigration screening and treatment of TB in children.

SHORT ABSTRACT SESSION

05. Improving diagnostics implementation: challenges and new solutions

SOA-539-29 Barriers to point-of-care testing in India and South Africa

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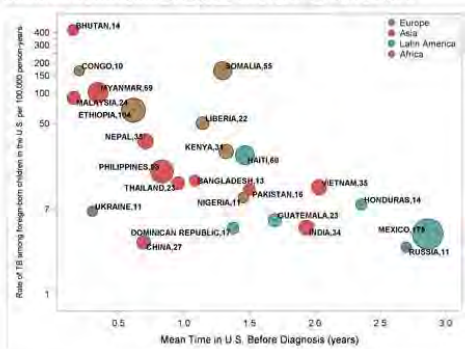
Background: Point of care (POC) testing promises to reduce delays in diagnosing and initiating treatment for diseases such as tuberculosis, HIV, syphilis and malaria. However, the availability of cheap, simple and rapid tests that can be conducted outside laboratories does not automatically ensure successful POC testing. In order to understand the challenges POC testing encounters, we need to study how tests are used at POC and integrated into workflow and patient pathways.

Methods: This paper reports on results from a qualitative research project on barriers to POC testing in urban and rural areas in India and South Africa. Using semi-structured interviews ($n=101$ in South Africa, $n=78$ in India) and focus group discussions ($n=7$ in South Africa, $n=13$ in India) with doctors, nurses, community health workers, patients, laboratory technicians, policymakers, hospital managers and diagnostic manufacturers, we examined diagnostic practices and the challenges in reaching a diagnosis across major diseases and actors in homes, clinics, communities, hospitals and peripheral laboratories. Data analysis was done thematically using qualitative data analysis software. While results per country have been published, this paper discusses selected results comparatively.

Results: The specific diagnostic eco-systems of South Africa (largely centralized testing with the exception of HIV screening) and India (largely peripheral testing spread across a multitude of actors) provide different conditions and challenges for POC testing. Patients embody active roles in managing their diagnostic journeys in both countries, albeit in different ways. The various strategies by providers and patients to overcome these challenges are fragile, ad-hoc and unsustainable. They can lead to further delays or poor outcomes.

Conclusions: It matters how technologies are used and made to work at POC. The contrasting results from India and South Africa highlight that settings and tests have their own histories, assumptions,

Figure 1. Rate of TB and average time in the United States before diagnosis by country of birth for foreign-born children, 2007–2014. Size of point is proportional to the number of cases occurring among children from that country. Countries of birth are labeled as follows: country name, number of cases reported among children from that country. Restricted to countries with at least 10 cases reported to NTSS among children aged <15 years.



and practices inscribed in them. This means that by implementing tests successfully both the setting, including its organization of the workflow, workforce, its infrastructure, interaction with patients and standards, and the tests are being shaped and need to be adapted. The paper concludes by reflecting on how to take such insights into account when designing POC testing programs for TB.

SOA-540-29 Task shifting in TB laboratory service delivery: the experience of non-laboratory technicians in two regions of Ethiopia

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Background: The USAID-funded HEAL TB project has been supporting comprehensive TB case identification, diagnosis and treatment services in two regions of Ethiopia. But some health centers were not doing Acid Fast Bacilli (AFB) microscopic service because of shortage of laboratory professionals; and pastoralist communities have limited access to health facilities. Nurses in non-diagnostic health centers and Health Extension Workers (HEWs) in pastoralist areas were trained in sputum collection, fixing sputum smears, and transporting of slides of presumptive TB cases. We present the results of this practice.

Intervention: A total of 457 nurses and HEWs (318 in Oromia and 139 in Amhara) were trained on TB symptoms and signs and the basic skills of collecting and fixing sputum smears. Nurses and HEWs transport the fixed sputum smear slides weekly to the nearest diagnostic health facilities. The diagnostic health facilities stain and read the slides.

Results and lessons learnt: A total of 8498 presumptive TB cases were identified either by nurses or HEWs from Jan-Dec, 2015. Three hundred twenty eight (4%) of the presumptive TB cases slides were referred by HEWs and the rest were by nurses. From the presumptive TB cases, 24,610 slides were processed at the diagnostic health facilities, and 519 slides were positive (Smear Positivity Rate [SPR]-2.11%). The rate of SPR is higher in Oromia compared to Amhara ($P < 0.05$). A total of 174 TB cases were diagnosed and initiated on anti-TB treatment. The SPR and yield among presumptive TB cases referred by HEWs and nurses was not significantly different ($P > 0.05$) [Table].

Conclusions: Use of non-laboratory professionals

in sputum slid smearing and fixing as well as with proper referral system could serve as an alternative approach to improve laboratory service accessibility.

Table Presumptive TB referral and yield of TB by HEWs and nurses

Indicators	Smear done by HEWs	Smear done by nurses	Total
Presumptive TB cases with slides smear fixed and sent	328	8170	8498
Total slides processed at diagnostic health facilities	900	23710	24610
Slide positivity rate (% , 95%CI)	3.00 (2.07-4.33)	2.07 (1.9, 2.26)	2.11 (1.93-2.29)
Yield of TB (% , 95%CI)	2.74 (1.34-5.33)	2.02 (1.73,2.35)	2.05 (1.76-2.38)

SOA-541-29 Field testing of TB sputum specimen optimizer (OMNI-gene) in Malawi, 2016

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Background: A key challenge to ensuring accurate TB diagnosis is transporting sputum samples to diagnostic laboratories without destroying the integrity of the sample by processing the specimen shortly after collection or storing it at a very low temperature. OMNIgene® is a reagent designed for liquefying and decontaminating sputum samples at the point-of-collection or in the lab while preserving *Mycobacterium tuberculosis* viability for at least 8 days at ambient temperatures (up to 40°C). The objective of this study was to evaluate whether OMNI-gene® can maintain the quality of sputum samples transported at ambient temperature from peripheral collection centers to centralized GeneXpert testing centers for improved case detection.

Methods: A comparative quantitative study conducted in six districts across Malawi (sample size 377). Two sputum specimens collected from presumptive TB cases were processed through two different sample storage and transport systems: one treated with OMNI-gene® and kept under ambient temperature ('intervention'); the other handled through regular cold chain ($< 4^{\circ}\text{C}$) storage and sample transportation system ('control'). All the samples were processed in the nearby GeneXpert center for the diagnosis of MTB.

Results: A total of 362 sputum samples were collected (96% of the expected sample size), with 47 (13%) of the samples excluded due to incompleteness. About 60% of the study participants

were females and the mean age was 42.3 years, with a range of 6 to 86 years. Preliminary data analysis showed a total of 30 (9.5%) *M. tuberculosis* positive cases identified in the 'intervention sample' and 32 (10.1%) identified in the 'control sample'. The intervention sample had 4 (1.3%) errors and 2 (0.6%) invalid reports, while the control samples had 9 (3%) errors. Cross tabulating the outcome of the 'intervention' and 'control' samples showed 97% agreement.

Conclusions: Preliminary results showed very high agreement between the control samples that went through standard cold chain process and the intervention samples that were treated with OMNI-gene®. This is very promising in countries like Malawi that face challenges maintaining cold chain for transporting samples from rural sites to central diagnostic laboratories.

SOA-542-29 Cost-effective technology improves distribution and management of logistics commodity for drug-resistant tuberculosis testing in Nigeria

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Background and challenges to implementation: The WHO ranks Nigeria 11th among the 27 high DR-TB burden counties in the world (Global TB report 2014). Diagnosis of drug-resistant TB relies on rapid molecular testing with Xpert MTB/RIF machines, but a systematized approach to country-wide GeneXpert cartridge management remains elusive. Several partners supporting the Nigerian Tuberculosis and Leprosy Control Program (NTBLCP) provide and manage GeneXpert machines with separate mechanisms. Cartridge distribution based on national requirements becomes skewed, and thousands of costly cartridges end up expiring in facilities that don't need them.

Intervention or response: Abt Associates and SystemOne developed and successfully piloted an innovative mobile-based solution (GxAlert) by networking laboratories across Nigeria. This low-cost system is configured on GeneXpert systems and an enabled wifi access in a dual-Sim router from a local tele communication that sends encrypted data on test results and cartridge logistics information to the secure web-based GxAlert database. The system's inventory management system forecast, track, and enable reallocation of usable GeneXpert cartridges across all networked sites.

Results and lessons learnt: This system Identified \$100k's of commodities that would expire before use; led to immediate reallocation and redesign of NTP logistics unit approaches to GeneXpert supplies. Real-time data are uploaded from GeneXpert systems through GxAlert, and SMS or text alerts are sent automatically to local, state and national logistics supervisors to show where cartridges are about to expire, when a facility has more cartridges than it can use within a particular period, and when a facility does not have the required number of cartridges based on the number of tests forecasted. Facilities in Nigeria with adequate cartridge supply based on forecasting with GxAlert jumped to 75% in January 2015 from 10% in April 2014.

Conclusions and key recommendations: GxAlert eliminates human error as cartridge forecasting is done automatically, pinpointing facilities that need immediate supply of cartridges as well as those that have more than they can use. GxAlert has strengthened and improve programmatic decision making for cartridge procurement, distribution and management. Based on these results, continued national rollout of GxAlert is recommended in Nigeria.

SOA-543-29 Electronic laboratory specimen (eSpecimen) referral system in Ethiopia: a feasible approach

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Background: Most health facility laboratories in Ethiopia are currently linked through courier services for sample transportation. However there was no well-established communication mechanism among the referring health facility (HF), the courier as well as the testing center (laboratory) in the tracking of sample referral, transportation and laboratory result delivery. We present the findings of the piloting conducted to assess the functioning of the web and mobile short message service (SMS) based sample referral & result delivery system.

Intervention: The USAID funded Help Ethiopia Address the Low TB performance (HEAL TB) project in collaboration with the Ethiopian Public Health Institute (EPHI) developed SMS & web-based laboratory information system. The eSpecimen system was piloted in 24 HFs that were linked to 24 couriers and 11 laboratories. HFs and laboratories enter patient information and laboratory results into the web system. The courier and the laboratory responsible for the referring HF receive alert whenever the HF pushes SMS/web based request. The courier delivers the specimens

to the laboratory. The HF gets the laboratory result via SMS, in the web system and also receives the hardcopy via the courier.

Results and lessons learnt: The web-based as well as SMS system functioned very well at the referring HFs, couriers as well as the testing centers. During the pilot, a request was made by HFs to transport 1217 samples (GeneXpert, Culture, DBS and viral load samples), 1132 (93%) were transported to the laboratory and laboratory results were ready for 695 (61%) samples. For GeneXpert sample with lower turnaround time, 82% of the cases have got their result in less than four days of sample delivery.

Conclusion: The pilot demonstrated that eSpecimen referral system is feasible and significantly improved the sample transportation and timeliness of laboratory result delivery.

Table Summary of samples handled in the pilot study

Request type	Samples requested <i>n</i>	Samples received <i>n</i> (%)	Results delivered <i>n</i> (%)
GeneXpert	282	232 (82)	224 (97)
Culture	693	658 (95)	411 (62)
Blood	242	242 (100)	60 (25)
Total	1217	1132 (93)	695 (61)

SOA-544-29 Increasing TB laboratory capacity: can we reduce the incubation time of MGIT?

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Background: Automated liquid culture systems for tuberculosis, like MGIT, are being scaled up globally, but TB laboratory capacity is limited by the protracted duration of culture; 6-weeks incubation is required to report negative results. This study evaluates whether MGIT incubation times may be reduced.

Methods: We analysed data on sputum smear positive adults enrolled in the international REMoxTB study. Samples were collected prior to and during TB treatment. Smear results, and results and times to detection for MGIT (TTP) and LJ (TTD) were recorded. Histograms depicting times to detection were created. Using different cut-offs for incubation time, sensitivity and specificity were calculated for MGIT to discriminate positive and negative results and evaluated using area under receiver-operating-curves (AUROC). Data were analysed in Graphpad PRISM and Stata₁₄.

Results: Data were available on 20,654 samples from 1928 patients prior to and during TB

treatment. The median TTP for MGIT is 11.33 [6.63-16.46] days and 28 [21-35] days for LJ. In MGIT culture, 90% samples have TTP < 21 days compared to 47% of LJ cultures with a TTD < 21 days. The AUROC for MGIT to discriminate between negative and positive results in either/or MGIT and LJ was 0.99. For pre-treatment samples, AUROC and sensitivity of MGIT culture to detect positives does not increase by prolonging incubation beyond 14 days (median 6+/-3 days; AUROC 0.99; sensitivity 99%). During treatment, reducing the MGIT incubation times results in an unacceptable loss of positive results. After 8 and 17 weeks of treatment, using even a 28 day cut-off, the sensitivity had fallen to 87% and 90% respectively. In areas where only MGIT culture, and not LJ, was available, 73 and 14 positive cultures, respectively, would have been missed.

Conclusions: For sputum samples collected for TB diagnosis prior to treatment, the sensitivity of MGIT culture does not improve by prolonging incubation beyond 14 days. Samples collected during treatment, however, require longer incubation. In routine practice, pre-treatment samples comprise the vast majority of samples tested globally; reducing incubation to 14 days may significantly increase TB laboratory capacity. Further research is required to evaluate these findings in smear negative patients.

SOA-545-29 Implementation of quality improvement project on Xpert[®] MTB/RIF utilization in a resource-limited setting of Nigeria using the Plan-Do-Check-Act (PDCA) Cycle

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Background and challenges to implementation: In June 2015, GeneXpert laboratories in Enugu State, south-east Nigeria recorded alarming rates of cartridge wastage for the first two quarters of the year. The number of tests with Error results and tests with invalid/incomplete results were seen to have increased within this period. Baseline data showed that Results with Errors were 6.0% (100) while tests with invalid/incomplete result were 12.2% (201) totaling 18.2% (301/1,653) wastage of GeneXpert cartridges.

Intervention or response: The intervention was to implement quality improvement activities in the laboratories using the Plan-Do-Check-Act (PDCA) framework. The plan was collectively drawn by the State TB program quality officers and testing laboratories in addition to Center for Clinical Care and Research Nigeria laboratory specialists.

Specifically, the PDCA cycle included: root-cause analyses; regular hands-on technical assistance; advocacy to hospitals' administration and monthly data monitoring. The objectives were to 1) reduce Xpert MTB/RIF cartridges wasted rate to below 10%, 2) reduce invalid/incomplete result rate to below 5%, and 3) evaluate the impact of PDCA cycle as a small test of change in improving utilization of GeneXpert cartridges. Data collection was carried out by the laboratory focal persons using the National Tuberculosis and Leprosy Control Program 'GeneXpert/MTB/RIF Quarterly report form'.

Results and lessons learnt: The intervention yielded a 12.6% overall decrease in number of Xpert cartridges wasted from 18.2% to 5.6%. The number of Error results reduced from 6.0% to 2.1% whilst the invalid/incomplete results decreased from 12.2% to 3.5% representing an achievement of the objectives (as shown in the table below).

Conclusions and key recommendations: Using the PDCA cycle to develop, implement, and monitor a work plan is an effective means of improving Xpert utilization through reduced wastage of cartridges. Collective effort and active participation of all key stakeholders is critical to the success of such interventions.

Table Xpert MTB/RIF cartridges before & after intervention

Xpert cartridges used	Baseline <i>n</i>	Baseline (%)	Intervention <i>n</i>	Intervention (%)
Error results	100	6.0%	34	2.1%
Invalid/ incomplete	201	12.2%	58	3.5%
Total wastage	301	18.2%	92	5.6%
Valid results	1352	81.2%	1,561	94.4%

SOA-546-29 Introduction of second-line drug-susceptibility testing services at the National TB Reference Laboratory of Swaziland

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Background: In Swaziland tuberculosis (TB) remains one of the leading causes of morbidity and mortality. The TB prevalence rate in Swaziland was at 907 per 100 000 population with multi-drug resistant (MDR) estimation of 7.7%. Since 2007 the National TB Reference Laboratory (NTRL) have only been performing 1st line drug susceptibility testing (DST) and 2nd line DST was

investigated in neighbouring countries. The NTRL conducted validation study with an aim to establish 2nd line DST service for early diagnosis of MDR-TB and subsequent improvement on result turnaround time and treatment outcome.

Methods: Between October 2014 to April 2015, the NTRL a conducted a validation process of 2nd line drugs which includes Kanamycin, Amikacin, Capreomycin, and Ofloxacin was performed against 20 TB positive isolates. All the 20 TB isolates were aliquoted into two parts and susceptibility testing conducted at both NTRL in Swaziland as compared to the results from a WHO and SANAS accredited Supranational Reference Laboratory (SRL) in Uganda. The DST was done using the MGIT 960 was independently performed in the two laboratories.

Results: The DST results from the NTRL compared to those from SRL in Uganda for Ofloxacin and Capreomycin were found to be almost perfect agreement with a Kappa value of 0.86 (0.60-1.00) and substantial agreement at a Kappa value of 0.78 (0.36-1.00) respectively. However, it was a perfect agreement for both kanamycin and amikacin. Taking the DST results at SRL of Uganda as a gold standard, the sensitivity & specificity of testing at the NTRL in Swaziland for both kanamycin & amikacin were 100% whereas the sensitivity & specificity of capreomycin was 100% and 95% and that of ofloxacin was 80% and 100% of respectively. The agreement rates obtained between the two laboratories and the observed sensitivity & specificity at the NTRL supports the introduction of the 2nd line DST in the country.

Conclusions: The introduction of 2nd line DST in the country expedited early diagnosis and reduction of result turnaround time with subsequent proper treatment of MDR cases. Furthermore, it enabled the National TB Control Program strengthens and improves drug-resistance surveillance and generates of data for policy decision making in Swaziland.

SOA-547-29 A qualitative evaluation of factors influencing adherence to the algorithm for TB diagnosis in primary health clinics in South Africa

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Background: The XTEND study, a pragmatic cluster randomised comparison of Xpert MTB/RIF vs. smear

microscopy for TB diagnosis reported no difference in mortality, nor time to treatment initiation, and highlighted the importance of addressing health system weaknesses in order to maximise the effect of new diagnostics. We investigated Xpert implementation and factors influencing adherence to the algorithm for TB diagnosis using Xpert at primary health clinics during the XTEND trial.

Methods: Semi-structured, in-depth interviews were conducted amongst 41 health care workers (TB co-ordinators, facility managers, TB nurses, primary care nurses and community health workers) at 8 primary care clinics of 40 participating in the XTEND trial. Clinics were selected to reflect the range of XTEND clinic geography, patient management, and TB investigation practice. Interviews explored informants' perceptions of Xpert efficacy as a diagnostic intervention, their role in implementation, and the collective actions at facility and health system level to achieve adherence to the algorithm. Attributes of clinics with successful and less successful Xpert implementation (defined by adherence to the algorithm for TB diagnosis) were identified.

Results: At clinics successful in implementation of Xpert, we observed 1) congruence between health care worker's perceptions of Xpert as an intervention to address the problem of TB in their community, and their understanding of the strengths and limitations of Xpert within the TB diagnostic algorithm; 2) key implementers (Facility Managers and/or TB nurses) who set clinic 'lore' of TB diagnosis that was fully adherent to the algorithm for TB diagnosis and who used their authority to streamline clinic processes accordingly; 3) functional and effective referral networks within and between clinics and district hospitals, including engaged technical support from clinic doctors, culminating in co-ordinated collective action to implement Xpert

Conclusions: Successful implementation of Xpert is associated with actions of key implementers who understand Xpert strengths and limitations, and who have capacity to organise TB diagnostic processes within their facility and local health care system in accordance with the Xpert diagnostic algorithm. When implementing new laboratory diagnostics, implementing agencies should identify, train and mentor key implementors to ensure maximal impact on patient and programme outcomes.

SOA-548-29 Connected diagnostics for tuberculosis programme support: from concept to reality

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Challenges: Connecting diagnostics through IT communications technologies can increase efficiencies

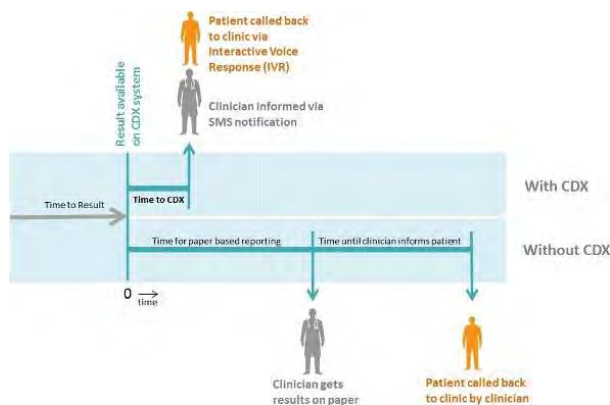
and lower costs for national TB programmes. Systems developed by manufacturers and third-parties have tended however to operate in isolation of other vendors' equipment, often located in the same laboratory or networks of diagnostic facilities. Systems to manage data from all diagnostic devices (e.g., GeneXpert, MGIT, line probe assay) would be desirable.

Intervention: FIND has developed the Connected Diagnostics Platform (CDP) for the centralised aggregation and management of data from multiple diagnostics belonging to different manufacturers. Currently, eight platforms from five manufacturers have been successfully inter-connected through the system, and others are in the process. The CDP reduces challenges associated with fragmented data sets by providing a common approach to data collection as well as providing tools to overcome constraints within health systems such as the timely reporting of results and their correlation from different diagnostic platforms to a single record.

Results: Initial testing of the CDP in Viet Nam, Peru and India has demonstrated benefits of having all test results in a common system that can quickly be enacted upon. In these evaluations four different instruments were connected to CDP across 9 sites: Cepheid GeneXpert, BD MGIT, Qiagen ESEQuant LR3 and Hain Genoscan. A total of 1912 results were collected. Traditional methods for reporting of results to the patient usually took 1-3 days if the laboratory was in the same facility as the clinician. However if the sample was referred, results were sent via mail usually taking between 5-10 days. During evaluation the CDP automatically sent SMS messages upon result availability to clinicians and mock patients reducing the effective reporting time to within 10 seconds. Tests performed on the same sample by different platforms were also seamlessly integrated.

Conclusions: Centralized programmatic information collected in real-time and quickly enacted upon provides an unprecedented opportunity to improve monitoring and generate new knowledge for enhancements in operational implementation, laboratory quality assurance, patient clinical management and epidemiological surveillance. Testing of CDP has shown positive initial outcomes and a number of national programmes and partners are engaged in its implementation and continued development.

Figure Connected diagnostics for TB



positive Pulmonary TB (B+PTB), six were smear positive. Of smear negatives four TB cases were diagnosed on Xpert and two on culture. Rifampicin resistance was detected in two cases (Figure). PTB was diagnosed in 4/56 (7.1%) patient having complaint of cough including one having cough for two weeks. Eight TB patient (3.3%) were diagnosed from among those with no complaint of cough. Taking into account five PTB cases on treatment (12+5/299) estimated prevalence of B+PTB in PWID is 5685/100K population.

Conclusions: In Pakistan HIV-infected injectable drug users having CD4 count less than 500 are at more than tenfold higher risk of getting tuberculosis and less than 10% complaint of cough which highlight the need for systematic active screening for TB in this key affected population

Figure Laboratory results of HIV patients screened

POSTER DISCUSSION SESSIONS

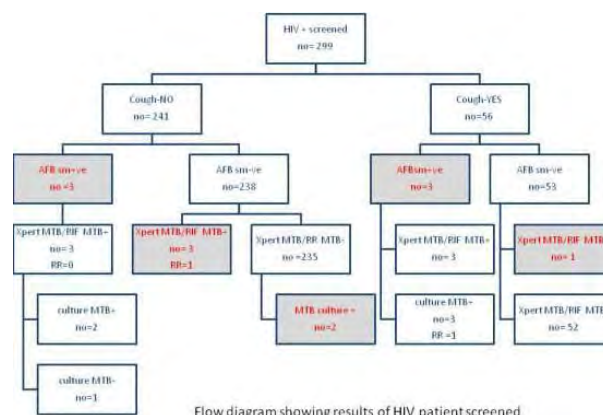
39. The 'rocky road' of screening and treatment outcomes

PD-994-29 Prevalence of TB in HIV infected injectable drug users having CD4 count < 500 admitted in detoxification centre in Islamabad

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Background: Pakistan, country moving from 'HIV low prevalence, high risk' to 'concentrated' epidemic mainly driven by people who inject drugs (PWID), with HIV prevalence at 27.2% (2011). Study is aimed to assess the prevalence of TB in HIV infected PWID. **Methods:** A cross-sectional study, all HIV infected adult male with CD4 count less than 500 admitted in detoxification centre were screened for TB. All were interviewed using short questionnaire on TB symptoms (cough, and fever), history of TB treatment and smoking. All were then guided to expectorate sputum. Sputa were tested in NRL using AFB smear microscopy on LEDFM, Xpert MTB/RIF assay and culture.

Results: Starting from June'15 to March'16, 339 HIV infected adult male were admitted and 299 (88%) of these were screened for tuberculosis with mean age 32.5yrs. 56 (18.7%) complaint of cough of any duration including 21 (7.0%) having cough for 2 weeks or more, 29 (9.0%) had past history of TB and five (1.7%) were on ATT and 91% were smokers. Twelve patients were diagnosed with bacteriological



PD-995-29 Enhancing TB detection and diagnosis amongst people living with HIV/AIDS utilizing peripheral TB laboratory service-delivery networks: experiences from Northern Nigeria

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Background: The rapid introduction of the GeneXpert technology with proven advantages over the microscopy method holds the promise to largely overcome current operational challenges as it reduces the turnaround time and improves the detection of rifampicin resistant TB strains. Although GeneXpert is the recommended first line diagnostic test for people living with HIV and re-treatment TB cases in Nigeria, the uptake is still very low in most of the center. This study aims to evaluate, the impact of linking GeneXpert labs with peripheral TB laboratory networks on TB diagnosis, in Northern Nigeria.

Method: The USAID funded proACT project implemented by MSH, in Northern Nigeria supports collaborative TB-HIV services at partner health facilities using a multi-disciplinary team approach. To address low uptake of GeneXpert services, 69 primary and secondary health facilities within 10-100km radius were mapped and clustered to feed in as spokes into 10 hospitals with GeneXpert capacity (hub and spoke model) between October 1 and December 31 2015. Capacity of health workers on the new technology and use of SOPs was built and a sample transport network that utilized LGA TBL Supervisors as couriers was initiated.

Result: Variables

	Before (Jan-Sep 2015)	After (Oct-Dec 2015)	% increase
Number of samples tested	1198	1270	6%
TB cases diagnosed	205	302	47%
DRTB cases	14	24	71%

Additionally results from 3 months prior intervention (Jul-Sep, 2015) compared to post intervention revealed 127% sample uptake ; 331% TB case detection and 1100% DRTB case detection

Conclusion: The introduction of a simple sample transfer System utilizing the Hub and spoke model improved TB case detection in Peripheral TB labs. To significantly increase TB case detection in Nigeria, peripheral and regional TB lab networks must be organized in such a way as to improve sample logistics to enhance patient access to early and accurate TB diagnosis, as this will potentially decrease morbidity associated with TB-HIV co-infection.

PD-996-29 Intensive screening for tuberculosis among people newly diagnosed with HIV in rural Cameroon

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Background: Bacteriological confirmation of TB in people living with HIV is hampered by generally lower rates of diagnostic test sensitivity than in those without HIV infection. Particularly in settings with high rates of HIV and TB co-infection, it is therefore important to assess the local TB prevalence and evaluate the diagnostic sensitivity of available laboratory methods to help guide clinician and program approaches to the diagnosis of TB.

Methods: Adults newly diagnosed with HIV at a

hospital in Northwest Cameroon were systematically tested for TB regardless of symptoms. All those who consented to participate were administered a demographics and symptom survey and received free CD4 testing and TB testing by smear microscopy and culture on both liquid (MGIT) and solid (LJ) media. Time to treatment initiation and patient outcomes were recorded following standard practice.

Results: Among 1,149 people screened, 940 were able to produce a sputum sample for microscopy and culture. Of those tested for TB, 68% were women, the median age was 35 years (IQR, 28-42 years), the median CD4 count was 291 cells/mL (IQR, 116-496 cells/mL), and 86% had a positive WHO symptom screen including one or more of current cough, fever, night sweats and weight loss. The prevalence of culture-positive TB was 13.6% (95%CI , 11.9-16.3%).

The sensitivity of direct smear microscopy in this population was 24.4% (95%CI , 17.9-32.4%) vs. culture. In comparison to those with smear-negative TB, patients with smear-positive TB had lower CD4 cell counts, more symptoms of TB and were more likely to have WHO stage3 or 4 disease (AIDS). However, while those with smear-positive TB had more advanced disease, those with smear-negative TB had a significantly longer delay to start treatment (26 days vs. 2 days) and poorer outcomes, with both higher rates of initial loss to follow-up and greater likelihood of death.

Conclusions: These findings highlight the need for the development and use of better diagnostic algorithms, as well as emphasis on careful patient follow-up. These activities will help to facilitate faster detection of TB cases and improve patient outcomes, particularly among people living with HIV who have smear-negative TB.

PD-997-29 Utility of urine as a clinical specimen for the diagnosis of pulmonary tuberculosis in people living with HIV

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Background: Tuberculosis is an opportunistic infection that increases the mortality and morbidity in human immunodeficiency virus (HIV) infected individuals. Despite the increased dissemination of tuberculosis among HIV infected patients, the diagnosis of pulmonary tuberculosis (PTB) by conventional three ZN stained smears examination shows negative smear. Due to low bacterial load in sputum specimen of HIV patients, using alternative specimens for increasing the detection rate of *Mycobacterium tuberculosis* is very important. Therefore, the aim of this study was to evaluate the utility of urine as clinical specimen for the diagnosis of pulmonary tuberculosis in people living with HIV.

Method: A cross-sectional study was conducted on PTB suspected patients infected with HIV from November 2013 to January 2015. A total 260 specimens were collected from 143 PTB suspected cases. The collected samples were processed for culture using L-J medium and the left were subjected to PCR using RD9 primers. All culture positive cases were subjected to spoligotyping for bearing in mind whether the isolated strain from both specimens the same or not.

Result: Out of 117 suspected PTB HIV infected individuals give both specimens, sputum culture alone detected more mycobacterial isolates 33 (28.2%) than the urine specimen alone 17 (14.5%). The detection rate of *M. tuberculosis* from urine in patients those who can't produce sputum (cough without expectoration) was 9/26 (34.6%). Of the 84 sputum culture-negative cases, four (4.8%) were urine culture-positive. Among patients whose pulmonary samples were negative by all bacteriological methods, the urine PCR was positive in 5.2% of the patients. The combination of urine culture and PCR result was comparable with the result of sputum culture with the sensitivity and specificity of 87.9% and 100% respectively. Out of 13 *M. tuberculosis* isolated from both sputum and urine of the same patients, 7 (53.8%) showed differ in their family.

Conclusion: PCR and culture examination of urine for diagnosis of suspected PTB in HIV infected patients were significantly improved the detection rate of *M. tuberculosis*.

PD-998-29 'Build it and they will come': additional diagnostic facilities increases the proportion of TB cases tested for HIV in Rajasthan, India

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Background and challenges to implementation: Of the estimated 9 million incident TB cases globally in 2013, about 13% were HIV co-infected. Of all TB-associated deaths, about 25% occurred among the HIV-co-infected. The World Health Organization (WHO) recommends offering routine HIV testing to all diagnosed TB patients. In 2014, 72% of about 1.4 million TB cases registered for treatment in India knew their HIV status. However, in Rajasthan, less than half of diagnosed TB patients knew their HIV status, due to limited number of HIV testing facilities available within general health care services.

Intervention or response: In 2013, to overcome this constraint, the Government of Rajasthan made a state-wide policy to set-up HIV diagnostic facilities at all peripheral health institutions (PHIs) which were not Integrated Counselling and Testing Centres (ICTCs) or Facility Integrated Counselling and Testing Centres (F-ICTCs) and to provide sputum smear-microscopy for Acid Fast Bacilli at all PHIs which were not Designated Microscopy Centres (DMCs). Number of sputum smear microscopy facilities in Banswara and Jhunjhunu districts increased from 33 and 22 before to 63 and 68 respectively after implementation of this policy; number of HIV testing facilities increased from 1 and 10 to 53 and 81 respectively.

Results and lessons learnt: In Banswara District, the proportion of TB cases tested for HIV was 22% and 49% respectively in the two periods. In Jhunjhunu District, the proportion of TB cases tested for HIV was 24% and 43% respectively in the two periods. Proportion of TB patients tested for HIV nearly doubled from the pre-intervention to intervention period. The proportion of registered TB patients tested for HIV from pre-intervention to intervention period were statistically significant ($P < 0.001$).

Conclusions and key recommendations: Our study shows that decentralizing of HIV testing facilities at all PHIs led to a greater proportion of HIV testing among persons with TB, which will ensure early access to HIV care services and may reduce both TB and HIV transmission and TB-HIV related mortality.

PD-999-29 Barriers affecting utilization of Xpert® MTB/RIF testing for tuberculosis in Cambodia

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Background: In 2012, the Cambodia National TB Program rolled out Xpert MTB/RIF testing for tuberculosis among people with presumptive MDR-TB and PLHA with presumptive TB in four northwest provinces. Findings from a programmatic evaluation showed Xpert utilization was low among the two populations, 37% and 51% respectively.

Methods: The Mixed Method analyzed data from: the quantitative programmatic evaluation; a self-administered structured response questionnaire (SRQ) ($n=62$); focus group discussions (FGD) ($n=6$) and in depth interviews (IDI) ($n=18$). Descriptive analysis of the SRQ and bivariate statistics were performed to compare survey responses to Xpert utilization at referring sites. Qualitative data analysis was facilitated via NVivo using a team-based directed approach.

Results: Barriers to Xpert utilization include clinicians' limited knowledge about the accuracy of Xpert

and the belief. 37% of SRQ participants stated Xpert testing was more accurate than smear microscopy, and only 53.2% said they always trusted Xpert results. Results aligned with themes identified in the interviews. A significantly high number of participants in both FGDs and IDIs reported that not all clinicians involved Xpert testing attended Xpert-related trainings. Clinicians perceived Xpert as an experiment, and as a likely error-prone TB diagnostic means. Barriers to optimal Xpert uptake included limited funds made available by the National TB Program (CENAT) to health facilities, to ensure TB suspects referral to district hospitals, and sputum transportation to Xpert sites. Health care seeking-related behavior and socio-economic conditions were additional barriers to high Xpert uptake that were reported by clinicians.

Conclusions: CENAT should provide more training on the Xpert testing performances and allocate sufficient funding for the patient's travel and the specimen's transportation to the Xpert sites.

PD-1000-29 The prevalence of HIV and tuberculosis and risk of mortality in adults with tuberculosis symptoms: a systematic literature review

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Background: The WHO recommends combined screening for HIV and tuberculosis (TB) among adults with symptoms of TB. There is need for better understanding of the benefits of and approaches for delivery of this combined screening at different levels of care. The objective of the systematic literature review was to investigate the prevalence of HIV and TB disease, and risk of early mortality among adults with symptoms of TB presenting at community, primary care, and hospital levels.

Methods: A systematic literature search was conducted in Embase, Global Health, Medline aiming for studies of HIV and TB screening in low and middle income countries published between 1 January 2003 and 1 January 2016. Study quality and heterogeneity were assessed; random effects meta-analyses were performed.

Results: Fifty three studies consisting of 556,962 participants were identified. The random effects weighted HIV prevalence among adults with symptoms of TB was 21.2% (95%CI 6.9–49.2) at community, 41.6% (95%CI 28.6–55.8) at primary

care and 77.9 (95%CI 70.8–83.7) among hospital inpatients. The pooled prevalence of TB disease was 0.7% (95%CI 0.3–1.9) at community-level, 26.3% (95%CI 17.8–37.0) at primary care level and 36.1 (95%CI 23.8–41.5) among hospital inpatients. The pooled mortality risk was highest among hospital inpatients, 20.3% (95%CI 13.0–30.1) at 1 to 3 months follow-up. Among those identified at the community and primary care, the mortality risk was very low, < 1% at 1 to 3 months.

Conclusions: There is higher prevalence of HIV than TB disease across all levels of care following combined screening. Combined HIV and TB screening can have greatest benefit of reducing mortality associated with HIV and TB among hospital inpatients in high prevalence settings.

PD-1001-29 Characteristics and treatment outcomes of extra-pulmonary tuberculosis patients in Kenya

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Background and challenges to implementation: Patients with extra pulmonary tuberculosis (EPTB) usually receive less priority in national TB Programmes. However, in many countries, their numbers remain either stable or are increasing while numbers of patients with pulmonary disease are decreasing. They usually represent 15% to 20%, or higher, of all TB cases in populations with low and higher HIV prevalence respectively. Diagnosis in many low-income countries is often based on presumptive and circumstantial evidence. In Kenya published information on EPTB is lacking, especially with regard to epidemiological characteristics and the most predominant forms. 'Treatment completion' is considered a successful outcome. Weight, a better gauge of successful treatment, is inconsistently recorded.

Intervention or response: We analyzed routine service provision data in the national case-based electronic data system, Tuberculosis Information from Basic Units (TIBU) for January 2013 to December 2014. Comparisons were made between EPTB and new smear-positive pulmonary tuberculosis (NPTB) patients. All 'transfer in patients' were excluded in the analysis.

Results and lessons learnt: Of the 109,223 patients, 31,636 (17.5%) had EPTB and 55.5% were males. Pleural effusion, lymph node and meninges tuberculosis accounted for 62.45% of all EPTB. Children < 15 years represented 13.3% of cases, with lymph node disease (43.3%) being most common among them followed by pleural effusion 14.6%. EPTB of the pericardium was the highest under 'EPTB other'. Less than 1% ($n=31,636$) of EPTB patients had a

confirmed diagnosis. There were 26,651 (84.2%) patients who successfully completed treatment. There was significant high proportion of deaths among EPTB patients (8%) compared to 3.8% among NPTB. The best treatment completion rates were in children < 15 years (88.1%) and only 4.2% died compared to 8.6% of adults. Patients with TB meningitis and millary had the worst outcomes. HIV positivity rate was 38.3% among EPTB and 87.6% ($n=12,128$) who were HIV co-infected were on antiretroviral therapy (ART). HIV positive status was associated with poor outcomes

Conclusions and key recommendations: Patients with EPTB generally do well in Kenya, although national TB Programme would benefit through more attention to accurate diagnosis, weight monitoring and earlier ART initiation in HIV-infected patients.

PD-1002-29 Effectiveness of treatment of patients with pulmonary tuberculosis combined with HIV infection

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Aim: to explore efficacy of treatment patients with combination of tuberculosis (TB) and HIV (TB-HIV), depending on presence or absence in complex treatment of TB antiretroviral therapy (ART).

Materials: The survey of 130 patients coinfecting TB-HIV who were on treatment in TB facilities of Saratov region in 2014. Among them: men - 93 (71.5%), women - 37 (28.5%). Age of examinees from 21 to 65 years. All patients were treated with anti-TB drugs (ATD) first and second row in accordance with detected drug-sensitive *Mycobacterium tuberculosis*. We shared TB-HIV patients at 2 groups. In Group 1 included 75 TB-HIV patients treated with ATD and ART. In Group 2 included 55 TB-HIV patients who received anti-TB drugs, but for various reasons it has not been carried ART. We evaluated efficacy completed course (intensive phase and continuation phase) of chemotherapy and analyzed before and after treatment number of CD 4 cells. The effectiveness of treatment of TB in patients TB-HIV assessed by dynamics of microbiologic, clinical and radiological data.

Results: The effectiveness of treatment of patients with TB-HIV presented in the Table. Efficiency of complex treatment of patients TB-HIV, depending on presence or absence in scheme of therapy antiretroviral drugs As the Table shows, effectiveness of treatment in patients of group 1 was significantly higher compared with group 2. In Group 1 patients after treatment ATD and ART also achieved an increase in number of CD4 (mean value of 301 ± 45 cells/uL) compared with original values ($202,3 \pm 32$ cells/uL), $P = 0,0432$. In patients Group 2 changes of this indicator has not occurred, the number of CD4

before therapy 343.8 ± 50 after treatment 327 ± 75 cells/uL, $P=0,8445$.

Conclusion: Efficiency of treatment of TB in patients coinfecting with TB-HIV was higher in patients from applying in complex treatment of tuberculosis anti-retroviral therapy.

Treatment outcomes of TB-HIV patients	Group 1 ($n=75$) Abs./%	Group 2 ($n=55$) Abs./%	<i>P</i>
Effective treatment	37/49.3	17/30.9	0.0416
Interrupted treatment	5/6.7	6/10.9	1.115
Died	17/22.7	26/47.3	0.0048
Ineffective treatment	16/21.3	6/10.9	0.1341

PD-1003-29 High mortality in tuberculosis patients despite HIV interventions in Swaziland

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Background: Swaziland has one of the highest TB incidence rates globally, and one of the highest generalized HIV prevalence in the world, at 31% among the 18-49 years old. According to the 2014 national TB report, 97% of TB patients were HIV-tested of whom 73% were co-infected with HIV. HIV has been shown to be the single most important risk factor for developing of TB, and to be associated with poor TB outcomes including high case fatality rates.

Aim: The aim of the study was to describe the impact of HIV interventions on the trend of TB treatment outcomes in 2010-2013 in Swaziland. The objective was to describe the evolution in TB case notification, uptake of HIV testing, antiretroviral therapy (ART) and cotrimaxazole prophylaxis treatment (CPT), and the proportion of TB-HIV co-infected patients with adverse treatment outcomes including mortality, loss to follow up and treatment failure.

Methods: This was a retrospective descriptive study using aggregated national TB program data.

Results: There was a decrease of 40% in the number of patients enrolled for TB treatment, from 11,057 cases in 2010 to 6,665 in 2013. The same trend was observed among the HIV positive TB patients. Over the four years, HIV testing uptake increased from 86% in 2010 to 96% in 2013. The coinfection rate remained stable at around 70%. Over 90% of the patients were prescribed CPT across the time period, at 93% in 2010 and reaching 99% in 2013. ART uptake increased from 35% to 75% over the study period. The proportion with adverse outcomes

amongst all notified TB-HIV patients decreased from 36% in 2010 to 30% in 2013. Mortality remained high, between 14% and 16% over the study period. Failure rates were stable over time (< 5%).

Conclusions: Despite high cotrimaxazole-prophylaxis and antiretroviral therapy uptake in TB-HIV patients, mortality remained high. Further studies are required to better define high risk patient groups, understand the reasons of death, and design appropriate interventions.

40. Childhood TB diagnosis and care detection

PD-1004-29 Increasing diagnosis of childhood tuberculosis in Swaziland: clinical utility of sample collection and diagnostic methods among children

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Background: Despite scientific and technological advances, TB remains an important cause of childhood morbidity and mortality globally. This research was approved by the MOH Scientific and Ethics committee and sought to investigate the utility of various methods for sample collection and diagnosis in order to improve diagnosis of paediatric TB in Swaziland.

Methods: A prospective cohort of 462 presumptive TB cases (ages 0-14 years) followed-up to confirm or exclude TB disease at two hospitals in Swaziland between January 2014 and August 2014. We collected urine samples, sputum samples by gastric lavage and mucus extraction, and blood samples. We evaluated the diagnostic accuracy of Xpert, Determine urine lipoarabinomannan (LAM) strip-test and mycobacterial blood cultures (Bactec) relative to TB bacteriological confirmation by MGIT. Data were entered using Epidata version 3.1 software, and STATA version 12.0 used for analysis. AUROC was calculated for TB LAM and Xpert laboratory results, relative to bacteriological confirmation.

Results: Of the 462 children enrolled, 78 (17%) were in-patients, 384 (83%) out-patients, 243 males and 216 females. Known HIV positive were 75 (16.2%), 71% reported TB contacts, 84% had two parents living, 249 were under 5 years, and 3% had Severe

Acute Malnutrition (SAM). We obtained 453 Sputum, 86 gastric aspirate, 426 urine and 462 blood samples. Of the 462 children, 4% (19) were bacteriologically confirmed TB cases (culture or smear positive) with 33% (5/15) of the culture confirmed cases diagnosed with drug resistant tuberculosis (DR-TB). The diagnostic accuracy of the urine LAM (sensitivity in HIV negative 17% and HIV positive 33%, specificity 86%, AUROC 0.61), XpertMTB/RIF (Sensitivity 16%, Specificity 100%, AUROC 0.58) to be low. All blood cultures were MTB negative. Odds of patients with self-reported asthma having TB were 2.9 times than in patients with. Gastric aspirates had higher positivity yield (5.5%) than extracted sputum (1.8%).

Conclusion: MDR-TB was common among the bacteriologically confirmed TB cases. Low sensitivity of Xpert was surprising but this combined with the high levels of otherwise unsuspected MDR-TB emphasise the need to strengthen clinical algorithms and use MGIT culture and DST on children to confirm presence and type of TB.

PD-1005-29 Yield of tuberculosis among children with presumptive TB using the Xpert® MTB/RIF assay in two regions of Ethiopia

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Background: Tuberculosis (TB) in children can be diagnosed by clinical/epidemiological assessment, bacteriologic confirmation, radiological finding or histopathology. In Ethiopia, GeneXpert is the preferred modality of investigation for children with presumptive tuberculosis. We present the diagnostic yield of TB among children with presumptive drug susceptible TB (DS-TB) and presumptive drug resistant TB (DR TB) in Oromia and Amhara regions.

Intervention: USAID-funded Help Ethiopia Address the Low Performance of Tuberculosis (HEAL TB) assisted in the purchase and installation of GeneXpert machines. The project trained health workers on childhood TB, provided cartridges, and established a sputum sample referral system.

Results and lessons learnt: A total of 3,885 sputum samples from children were sent and tested at 49 GeneXpert sites in Oromia and Amhara regions (81.8% presumptive DS-TB and 18.2% presumptive DR-TB). TB in children was confirmed in 457 (11.8%) cases of which 0.4% and 11.3% were RR-TB and DS-TB, respectively. 10 RIF resistance were identified from DR-TB suspects while 5 were from DS-TB suspects. The overall yield of all forms of TB and RR TB among children was less than the yield among adults ($P < 0.05$). There is no significance

difference in terms of the yield of TB with in the categories of presumptive DR TB and presumptive TB cases ($P>0.05$) (Table). The introduction of GeneXpert in the diagnosis of TB in children is a significant breakthrough that increased the quality of TB diagnosis in children and also enabled the diagnosis of DR TB.

Conclusion: The overall diagnostic yield using GeneXpert among children is comparable with the 13% yield in high HIV prevalent setting in South Africa. GeneXpert has detected a significant number of TB cases in children including RIF-Resistant cases which could have been missed without the introduction of GeneXpert.

Table Yield of TB among children

Variables	Total n (%)	Age <15 years	Age >15 years	Proportion test (P -value)*
Samples tested by GeneXpert	28 726	3885	24 841	NA
TB cases identified overall (% yield)	4586 (16%)	457 (11.8%)	4129 (16.6%)	0.008
Yield among presumptive MDR-TB cases	2482 (22.01%)	119 (16.8%)	2363 (22.4%)	0.151
Yield among presumptive TB cases	2436 (14%)	387 (12.2%)	2049 (14.4%)	0.253

PD-1006-29 Effective testing for pulmonary TB in children using stool specimens using the Xpert® MTB/RIF assay in Pakistan

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Background: Childhood tuberculosis (TB) is largely paucibacillary disease and difficult to diagnose. In the absence of sputum or gastric aspirate (GA) based testing, patients largely remain undiagnosed and treatment is often given empirical. In this study we used Xpert® MTB/RIF testing for *Mycobacterium tuberculosis* in pediatric pulmonary TB cases by performing comparative testing of gastric aspirate and stool samples.

Methods: We recruited children suspected of TB from the Department of Pediatrics, Civil Hospital, and The Aga Khan University Hospital, Karachi. Patients were evaluated using a modified Kenneth Jones (KJ) TB score ≥ 5 . Paired GA and stool samples were collected from 48 patients who met the study criteria. The Xpert assay (and *M. tuberculosis* culture was performed on all gastric aspirates.

Results: A total of 27 male and 23 female children were recruited into the study, with a mean age of 6

years and a mean TB (KJ) score of 7. The rate of TB detection based on TB Xpert testing of GA was 22% (11 cases). The rate of TB detection *M. tuberculosis* culture of GA was 21% (10 cases). The rate of TB detection based on TB Xpert testing of stool samples was 21% (10 cases). No rifampicin resistance was detected. Hence, we found concordance between Xpert TB testing of GA and stool in all but one case. In one case, there was a low positive GA Xpert and positive *M. tuberculosis* culture but a negative stool Xpert result. In another patient, there was a low positive GA Xpert and *M. tuberculosis* culture and positive stool Xpert. All 11 cases of TB diagnosed were put on anti-tuberculous therapy and responded well to treatment.

Conclusions: Our data indicates that in children with TB, positive Xpert *M. tuberculosis* stool tests were associated with a higher TB score (> 5) and when the bacillary load is higher, with a strong positive Xpert result. In a resource poor setting where it is difficult to perform complex testing such as gastric lavage, testing for TB in stool using the TB Xpert assay may be a valuable and non-invasive diagnostic alternative.

PD-1007-29 Perceptions of health workers towards sputum sample collection from children for the diagnosis of tuberculosis in Uganda

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Background: Attainment of sputum samples is one of the cornerstones of tuberculosis (TB) diagnosis, yet younger children often cannot expectorate sputum. The collection of sputum from children requires knowledge and skill. The application of this skill may be influenced by health workers' attitudes and perceptions. We conducted a practical training on sputum collection from children for health workers in Uganda and explored the perceptions of health workers towards the training and towards the sputum collection techniques.

Methods: This was a qualitative study using document content analysis. Following the training, each health worker completed an evaluation form including Likert scale and open-ended questions assessing their perceptions towards the training and sputum collection procedures. Trainers also wrote training reports on their observations. The training included health workers from 29 health facilities in five districts of Uganda between June-December 2014. Each training session lasted three days and included

four participants. The participants were trained on three sputum sample collection techniques: gastric lavage, laryngopharyngeal aspiration and sputum induction.

Results: A total of 87 health workers underwent training and completed evaluation forms (response rate 100%). A conventional content analysis approach of the evaluation forms and training documents identified several emergent themes, including: health worker knowledge gaps on approaches to attain sputum samples from children, health worker skill gaps on sputum collection procedures, misconceptions regarding the equipment or environments required for sputum collection, health worker satisfaction with practical skills-based training, and health worker eagerness to learn. Several participants commented that the procedures for sputum collection in children were easier to perform and better tolerated by children and caregivers than they had expected. Many participants perceived that laryngopharyngeal aspiration was technically easier to perform compared to sputum induction and gastric aspiration.

Conclusions: The findings suggest that health workers are eager to improve their skills in this area and suggest that with practical training, health workers can gain confidence to better collect sputum samples from children. This study identified knowledge and skill gaps as well as misconceptions that pose barriers to childhood TB diagnosis. The laryngopharyngeal approach for collecting sputum was well accepted.

PD-1008-29 Improving detection of tuberculosis through active case finding among children attending informal schools in urban informal settlements in Nairobi

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Background: Detection of TB among children remains a challenge with many cases undiagnosed. Childhood TB is closely associated with poverty, crowding, and malnutrition. 80% of Nairobi residents in Kenya, live in the informal settlement and a significant proportion of children attend informal schools which are well known to fuel infectious disease transmission. An assessment was conducted to determine the effect of ACF in diagnosing TB among children attending these schools.

Methods: A cross sectional assessment was conducted from 9-16 March 2016 among children attending 174 informal schools in the informal settlements in

Nairobi. All children aged < 14 years were screened for symptoms of TB using the Simplified Pediatric TB Diagnosis tool recommended by the Kenya Ministry of Health. Where possible, sputum samples from those with presumptive TB were sent for Xpert MTB/RIF testing. Mantoux test and chest x-rays were unavailable. Children were assessed for malnutrition using MUAC. Data was analyzed to determine the prevalence of TB following this approach to screening in high risk populations.

Results: A total of 11,148 children were screened and the majority, 49%, were < 5 years of age while 41% were 5-9 years of age. On assessment, 4% of the children had malnutrition. Overall 496 (4.4%) of these children were found to have TB using the national diagnostic tool. Of the 193 (39%) children who produced sputum for Xpert, none were positive for *Mycobacterium tuberculosis*. Malnutrition was found in 92% of children with TB compared to 19% among those without.

Conclusions: Active TB case finding Diagnosis among high risk children is an effective tool in improving TB diagnosis among this vulnerable group. Sputum production for GeneXpert testing among children remains challenging calling for the need for scale-up of other equally effective tests in addition to training health care workers on more aggressive interventions including sputum induction to improve TB diagnosis in children. For this children Xpert did not pick any *M. tuberculosis* as compared to the simplified Pediatrics TB diagnosis tool hence more research need to be done on specificity and sensitivity of our simplified pediatric diagnosis versus Xpert and the quality of specimen from children.

PD-1009-29 Evaluation of the Xpert® MTB/RIF assay in children with presumed pulmonary tuberculosis in Papua New Guinea

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Background: The Xpert® MTB/RIF assay is used for the detection of *Mycobacterium tuberculosis* and rifampicin (RIF) resistance. We aimed to determine the yield of Xpert and assess its performance in children with presumed pulmonary tuberculosis (PTB) in Papua New Guinea (PNG).

Methods: Children admitted to Port Moresby General Hospital, PNG, with presumed PTB were enrolled in this prospective study, and classified as probable, possible, and unlikely TB. Sputum or gastric aspirate

(GA) were collected and tested with Xpert and the standard acid fast bacilli (AFB) smear. Children were diagnosed and treated for TB based on standard diagnostic criteria which were used as the primary reference standard. The results of Xpert, AFB smear and the Edwards TB score were compared to this primary reference standard. Culture and DST were done on a subset.

Results: Ninety-three children ≤ 14 years were enrolled; 72% (67/93) were classified as probable, 22% (21/93) possible and 5% (5/93) TB unlikely. Sixty-two GA and 31 sputum samples were obtained. Eighty children were treated for PTB based on the primary reference standard. Xpert detected MTB among 26/93 (28%) of cases, including 33% (22/93) with probable TB, and 19% (4/93) with possible TB. Xpert detected rifampicin resistance in 13% (13/93) of samples; of these, phenotypic drug sensitivity testing detected rifampicin resistance in two. The yield of Xpert greater than AFB testing (26 v 13 positive results, $P=0.019$). AFB smear detected *M. tuberculosis* in one case which was Xpert negative but culture positive. The sensitivity of Xpert, AFB smear and an Edwards TB score of ≥ 7 compared to the primary reference standard was 31% (25/80), 16% (13/80) and 90% (72/80), respectively. The specificity of Xpert, AFB smear and an Edwards TB score ≥ 7 was 92% (12/13), 100% (13/13) and 31% (4/13), respectively.

Conclusion: Xpert augments clinical decision making and identifies rifampicin resistance, but the sensitivity remains suboptimal. A negative result does not rule out TB in children. Hence, in TB high burden settings diagnosis of childhood TB remains reliant on thorough history, rigorous standardized clinical criteria, and CXR. Practical guidelines should be used to identify children who would benefit most from Xpert.

PD-1010-29 Increasing childhood TB notification through systematic screening in public-sector hospitals in rural Pakistan: an update

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Background and challenges to implementation: The burden of tuberculosis in children is underestimated due to under diagnosis and inaccessibility of care. Active screening is known to increase adult TB case finding and notification in urban and rural settings.

Intervention or response: Screeners trained on using android based interactive algorithms, screened chil-

dren at the pediatric outpatient departments of four large public hospitals in Jamshoro district, Sindh, from Quarter 4, 2014 to date. Children with one or more symptoms of TB (cough ≥ 2 weeks; contact history of TB or a combination of two of following: fever ≥ 2 weeks, night sweats or weight loss) were referred to a medical officer who clinically evaluated and ordered diagnostic tests including chest X-ray, AFB smear, and Xpert assay. All tests were offered free of cost. Diagnosed children were started on TB treatment and caregivers were asked to bring other children in the household for screening.

Results and lessons learnt: Screeners verbally assessed 87,781 children between October 2014 and December 2015, of which 4,347 were classified as presumptive TB suspects; 1057 were diagnosed with TB with 468 (44%) females, 521 (49%) between 0 to 4 years of age and median age 5 years. Majority 847 (80%) had pulmonary TB and the overall prevalence of TB was 1.2% of all children screened. 1261 child contacts from 521 index patients were contact traced, 137 were found to have the disease; 57 (42%) females; median age of 4 years and 125 (91%) had pulmonary TB. The prevalence of disease amongst contacts was 10.8%. These activities resulted in an over 3 folds increase in pediatric TB case detection and notification compared to previous 5 quarters in the intervention district. No change in pediatric TB case notification was reported in control district.

Conclusions and key recommendations: Active screening at pediatric outpatient departments of rural hospitals can increase child TB detection and notification many fold. Higher case detection in the 0-4 year age group in our rural setting likely occurred because of the integration of TB screening with the EPI program, resulting in earlier TB detection in this vulnerable group.

PD-1011-29 Reaching missing paediatric TB cases through contact tracing: experience from sixty districts in India

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Background and challenges to implementation: Close contacts of TB cases, especially Paediatric age group, are highly vulnerable towards developing TB. However, active contact tracing of close contacts of TB patients is not yet part of the strategy under Revised National TB Program (RNTCP) in India leading to loosing early detection of TB among Paediatric age group.

Intervention or response: Population Services International (PSI) implemented an intense outreach activity for tracing Paediatric contacts of TB patients in selected Tuberculosis Units (TUs) across 60

districts in India as part of Project Axshya. Community based volunteers were recruited for conducting household visits of TB patients registered under RNTCP during the period July 2013-December 2013. Community volunteers identified children and persons with symptoms of TB from the close contacts of TB patients and linked them for TB diagnosis and treatment with RNTCP services. The child contacts of TB patients were also linked to INH prophylaxis.

Results and lessons learnt: A total of 12,126 TB patients were registered during July - December 2013 in 120 Tuberculosis units (TUs) across 60 intervention districts. Community volunteers reached around 8,425 (70%) of households of listed TB patients (12,126). Of the 5,866 children under 6 years screened, 155 were TB symptomatic and 38 of the symptomatic were found positive and linked to treatment. 1,489 children were linked to INH prophylaxis through the intervention.

Conclusions and key recommendations: Contact tracing of TB patients helps to detect the TB among Paediatric patients and link them to diagnosis and treatment. The overall positivity rate among Paediatric symptomatic was 24%. Contact tracing should be included as a routine activity under the RNTCP program in India to detect and treat paediatric TB.

1012-29 Targeting missed opportunities for childhood TB management integration in Nigeria using comprehensive OVC programs: PEPFAR/USAID/FHI360 experience

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Background: Despite the considerable burden of childhood-TB, it is still a neglected aspect of most National TB Programs. Nigeria has the highest burden of orphans and vulnerable children (OVC) due to HIV/AIDS epidemics in the world, and the actual burden of TB disease amongst these underserved population is unknown. Lack of family-centred contact tracing, as well as guidelines on systematic screening, referrals of presumptive-TB cases and TB diagnostic tools for children hinders early detection and effective childhood-TB management at the community level.

Methods: A retrospective data analysis of children aged 0-17 years, either infected or affected by HIV/AIDS, enrolled into the PEPFAR/USAID funded Strengthening Integrated Delivery of HIV/AIDS Services (SIDHAS) OVC program between October 2014 and January, 2016 in 13 supported states in Nigeria was done. The childhood-TB symptoms

screening checklist of cough, fever, weight-loss, night-sweats and lymphadenopathy was incorporated into the child status index (CSI) OVC intake and follow-up forms. The CSI-form is used to assess individual needs at intake, make service provision careplans and monitor outcomes. Other activities carried out included advocacy to relevant government agencies, sensitization of community leaders and capacity building of health-facility staff, policy makers, health-care workers, and community volunteers using an integrated-TB training curriculum. Data-analysis was by SPSS-16.

Results: Records of a total 3521 children screened for TB were analyzed. Five hundred and twenty eight (528 = 15%) were presumptive-TB cases, and were referred to health facilities for diagnosis by GeneXpert, sputum AFB microscopy and chest X-ray. Two hundred and six (206: 58 females & 148 males), 39% of the total children referred were diagnosed with TB disease, and were started on anti-TB treatment in supported facilities. The children not positive of TB were referred for further assessment and those eligible for prophylaxis were placed on isoniazid preventive therapy (IPT).

Conclusions: Incorporating childhood-TB symptoms screening checklist into the CSI assessment and monitoring tools for OVC programs using existing frontline community stakeholders is helpful in increasing referrals of presumptive-TB, and childhood-TB case detection. It can also provide opportunities for TB-prophylaxis among those without active TB. This approach should be recommended in countries with high TB-HIV burden.

PD-1013-29 Tolerability of the string test for tuberculosis diagnosis in children aged 4-14 years

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Background: Bacteriological confirmation of tuberculosis (TB) is rarely achieved in children because often they are unable to produce an adequate sputum sample and/or have paucibacillary disease. The World Health Organization highlights the importance of the development of new strategies for diagnosing TB in children. The string test is one non-invasive alternative to sputum-based diagnosis of TB, however, previous studies have shown contradictory results with regard to its tolerability in children. We examined the tolerability and feasibility of the string test in a group of Peruvian children suspected of having TB.

Methods: We enrolled 29 children (4 to 14 years old) with TB symptoms and a household contact. Partic-

ipants were asked to swallow a gelatin capsule with an attached nylon string. One end of the string was adhered to the cheek, and the child was asked to swallow the capsule, which was 1.5 to 2 centimeters in length depending on the child's age. The string remained in the stomach for up to four hours before it was removed and underwent culture for *Mycobacterium tuberculosis* using BACTEC MGIT. Success rates and common events were recorded electronically using a standardized form.

Results: Of 29 children, the string test was completed successfully in six (21%), ranging in age from 5 to 13 years (median=9 years). Of the children who completed the string test, five of them had negative culture results from both the string sample and either a sputum or gastric aspirate sample; one child did not yet have available culture results. One of six children with a successful test experienced retching during string intra-gastric downtime. Of the 23 children unable to complete the test (79%), one was 14 years old, and 22 were between 4 and 10 years old. Reasons for non-completion were (categories not mutually-exclusive): difficulty swallowing (56%), vomiting (19%), anxiety (19%) and retching (4%).

Conclusions: Tolerability and feasibility of string test is low in children between 4 and 10 years old years old: more than half were unable to swallow the capsule. Decreasing the capsule size may improve the tolerability and feasibility of the string test in this group.

41. Latent TB infection testing: who and how

PD-1014-29 Risk factors for active tuberculosis in human immunodeficiency virus co-infected tuberculosis contacts, Taiwan

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Background: People living with human immunodeficiency virus (PLHIV) have higher risk to develop active tuberculosis (TB) even receiving antiretroviral therapy (ART). Evaluating TB risk among HIV co-infected contacts is needed for countries with moderate TB incidence, low HIV prevalence, and free ART care to expand latent infection treatment in TB control program.

Methods: We conducted a cohort study in HIV co-infected TB contacts from TB registry during 2005-2012 and followed till December 31, 2014 for reporting of active TB. We also used individual identification number of contacts to cross-link with both the nationwide HIV surveillance system and national health insurance (NHI) claims database to

collect baseline demographics and covariates known as risk factors of TB. We also calculated the TB incidence of participants and used Cox proportional hazard model to estimate the hazard ratio (HR) and 95% confidence interval (CI) for the association of TB risk and HIV status among contacts.

Results: A total of 621 HIV co-infected contacts were enrolled. Most of the participants were male (93%), the median age was 35 (IQR: 30-42), and 39% of HIV contacts initiated ART before or within 6 months after TB exposure. None of 621 contacts received isoniazid preventive therapy (IPT). There were 14 contacts developing active TB after the median follow-up duration of 3.76 (IQR: 2.58-5.52) years. The overall TB incidence was 551.88/100 000 (314.10-904.00) person-year. In multivariate analysis, cavitation lesion on chest X-ray of index case (aHR: 3.59, 1.11-11.62), co-morbid chronic obstructive lung diseases (aHR: 7.07, 1.46-34.12) and utilization of outpatient service ≤ 2 times in one year (aHR: 5.95, 1.1-31.78) were associated with TB disease after controlling ART use, CD4 counts at TB exposure, and using injection drugs. Hazard of active TB in HIV co-infected contacts who initiated ART before or within 6 months after TB exposure did not significantly differ from those without ART. ($P=0.907$, by log-rank test).

Conclusions: HIV co-infected TB contacts had 11 times of higher risk to develop active TB than general population in Taiwan. Enhancing IPT in PLHIV, especially in HIV co-infected TB contacts regardless of initiating ART could further reduce the TB incidence.

PD-1015-29 Diagnostic specificity of immunological methods in diagnosis of the tuberculosis and latent tuberculosis infection among children

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Background: IGRA-tests - modern methods of latent TB infection diagnosis; their positive results are associated with the process of active reproduction of *M. tuberculosis*. One such method is T-SPOT.TB, has used in the world since 2004. In Russia this method was licensed in 2012, but results of T-SPOT.TB utilization among children are not presented in publications.

Objective: To compare the diagnostic specificity of T-SPOT.TB and tuberculin skin test (TST) for diagnosis of LTBI among children.

Methods: 92 patients from 3 to 14 years old were examined and included in open cross-sectional study

at children's departments during 2014-2015. All patients were vaccinated by BCG. Diagnostic complex included: clinical, immunological (tuberculin skin test (TST), T-SPOT.TB), and radiological methods (computed tomography). After examination 2 children were diagnosed with tuberculosis of intrathoracic lymph nodes, 3 children had latent TB infection, and 87 - healthy children. 62 children (67.4%) had concomitant allergic diseases (24 - asthma, 11 - atopic dermatitis, 7 - hay fever, 1 - urticaria). Indicators of diagnostic specificity (DSp) of TST and T-SPOT.TB were calculated. Statistical analysis was performed using Graph Pad Prism 6. The χ^2 test was applied.

Results: Results of TST were as follows: children with LTBI ($n = 3$) and TB ($n = 2$) demonstrated positive results; healthy children ($n=87$) - in 77% ($n=68$) had high results (≥ 15 mm), 17.2% ($n=15$) - medium results (10-14 mm), 5.8% ($n=5$) - low results (< 10 mm). Results of T-SPOT.TB were negative in all 87 healthy children. Results of T-SPOT.TB were positive in 2 children with TB and two children with LTBI. In one child with LTBI negative result was observed. Diagnostic specificity was following: T-SPOT.TB (100%), TST (23%).

Conclusions: T-SPOT.TB has high diagnostic specificity in comparison with TST in diagnosis of TB and LTBI in children with allergic pathology that can be applied in clinical practice.

PD-1016-29 T-SPOT performance in routine pediatric practice in a low TB burden setting

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Background: The T-SPOT.TB test, an interferon-gamma release assay (IGRA), is a test of tuberculosis infection (TBI). Due to conflicting and limited data, the American Academy of Pediatrics recommends use of IGRAs in children > 2 years of age, cautioning that negative or indeterminate tests do not rule out TBI. We analyzed T-SPOT.TB results to determine the prevalence of invalid, borderline, positive, and negative results and associations with key demographic variables.

Methods: Oxford Immunotec provided de-identified initial T-SPOT.TB results for 44,289 children < 17 years of age whose samples were received at Oxford Diagnostic Laboratories from 2010-2015. The associations between test outcome and demographics

(age, sex, draw site) were estimated by bivariate analysis and logistic regression.

Results: Among the 44,289 samples, tests were not performed on 592 (1.3%) due to laboratory technical error or sample-specific factors and were not associated with patient characteristics. An invalid test due to a low mitogen response was uncommon (0.2%, 86/44,289) and not associated with age, gender or draw site. An invalid test due to a robust nil response was uncommon (0.4%, 168/44,289) and associated with younger age and HIV clinic draw site. Compared to a negative response, positive responses were more likely in samples from older children ($P < 0.0001$) and public health draw sites ($P \leq 0.0001$). Younger children were more likely to have borderline than negative results ($P < 0.0001$), but there was no difference in the odds of positive compared to borderline results.

Conclusions: Technical errors or sample-specific factors rarely prevented sample testing regardless of patient's young age or shipping requirements. Rare invalid results due to robust nil control responses were associated with young age potentially due to an immature immune response. Rare invalid results due to a weak positive control response were not associated with age or HIV draw site, illustrating that anergy was not common in patients screened for TBI in our study population—including those with HIV-infection. Younger age was associated with borderline results, but at clinically insignificant levels, supporting use of IGRAs in young children. Differential positivity rates across draw sites suggest that targeted IGRA use should consider the population's pre-test probability of TBI.

PD-1017-29 Pregnancy-associated decreased TST vs. QFT positivity and lower QFT mitogen and *Mycobacterium tuberculosis* antigen responses compared to postpartum in HIV-infected women

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Background: Pregnancy may influence latent TB infection (LTBI) diagnostic performance, potentially due to immunologic changes. Longitudinal studies of tuberculin skin tests (TST) and QuantiFERON® (QFT) among HIV-infected peripartum women in sub-Saharan Africa are lacking.

Methods: As previously described, we performed QFT and TST on 96 HIV-infected women enrolled antenatally in western Kenya, and repeated QFT/TST testing at 6 weeks postpartum in 86 women (excluding 10 who were QFT+/TST+ in pregnancy). QFT Mtb-Ag ≥ 0.35 IU/mL and TST ≥ 5 mm were considered positive. QFT identified more women with LTBI than TST in pregnancy (QFT 34.4% vs. TST 13.5%, $P=0.006$) and postpartum (QFT+ 29.5% vs. TST+ 14.1%, $P<0.0001$). To further investigate potential immunologic effects of pregnancy on LTBI testing, we compared QFT quantitative Mtb-Ag and mitogen stimulated IFN- γ responses by peripartum stage and QFT/TST result.

Results: At baseline in pregnancy, mean Mtb-Ag IFN- γ was non-significantly higher among QFT+/TST+ (10/96) vs. QFT+/TST- (23/96) (4.90 vs. 3.74 IU/mL, $P=0.39$). Of 86 women QFT-tested both in pregnancy and postpartum, mean Mtb-Ag and mitogen IFN- γ response were lower in pregnancy vs. postpartum (Mtb-Ag: 1.03 vs. 1.54 IU/mL, $P=0.03$; mitogen: 4.46 vs. 7.64 IU/mL, $P<0.0001$). Among 22 women who were QFT+ both in pregnancy and postpartum, mean Mtb-Ag IFN- γ response was significantly lower in pregnancy (3.46 vs 4.48 IU/mL, $P=0.007$). Excluding 4 women without TST results, 10 QFT+/TST- pregnant women remained TST- postpartum, with lower Mtb-Ag IFN- γ response in pregnancy vs. postpartum (3.59 vs. 5.08 IU/mL, $P=0.09$). Eight QFT+/TST- women converted TST+ postpartum, with non-significantly lower Mtb-Ag IFN- γ in pregnancy vs. postpartum (4.01 vs. 4.92 IU/mL, $P=0.19$). Most (41/44) QFT-/TST- pregnant women remained QFT-/TST- postpartum, without change in Mtb-Ag IFN- γ (0.04 vs. 0.04 IU/mL $P=0.93$). Three had LTBI test conversion postpartum. One converted to QFT+/TST+ (Mtb-Ag IFN- γ increased from 0.03 to 8.07 IU/ml postpartum); 2 converted to QFT+/TST- (mean Mtb-Ag IFN- γ increased from 0.0 to 2.33 IU/mL).

Conclusions: Although QFT has higher diagnostic sensitivity for LTBI than TST during pregnancy and postpartum, lower Mtb-Ag and mitogen IFN- γ responses in pregnancy suggest that immune changes of pregnancy may influence both QFT and TST test performance.

PD-1018-29 Latent TB in patients with chronic renal failure: results from a national survey

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Background: Patients with chronic renal failure are especially prone to infections due to dampened adaptive immunity. Tuberculosis (TB) in particular poses a significant risk including the potential for anti-TB drugs to further worsen the prognosis of patients. It is thus imperative that TB is diagnosed in a timely fashion in these patients to ensure an early adaptation of drug regimes that minimise risk. This national survey was carried out to assess nationwide burden, awareness and management of TB in chronic kidney disease (CKD).

Methods: We designed a survey using a web based source, Survey Monkey and disseminated to all the renal units in the UK. The questions in the survey were designed to assess incidence of tuberculosis in CKD patients, any potential bias in population groups, the frequency of screening and whether anti-TB therapy was offered in the clinic.

Results: A total of 43 responses were received from renal dialysis units from England, Scotland and NI. Of these, 40% also offered renal transplant to patients. A vast majority of the centres (93%) reported a low incidence ($<5\%$) of TB in CKD patients over a period on one year. However, surprisingly the majority of centres (95%) did not routinely screen CKD patients for latent TB. Many (70%) also did not screen for TB in patients with specific conditions (CKD4 and 5 and transplant patients). The country of birth (endemic TB areas) played an important role in screening decisions for some units, however only 3% of the respondents considered screening in people with social risks. A vast majority then referred the cases to a local TB service (95%), however a similar number (91%) were also unaware for the transmission of TB within their units.

Conclusions: Latent TB screening was carried out infrequently across the renal units in the country. However screening did occur in patients with CKD 4 and 5 who were born outside UK. While, there is a national guidance for treatment of TB in patients with chronic renal failure, its implementation is not robust due to poor awareness. Most units correctly referred patient to local TB services.

PD-1019-29 Micronutrient supplementation augments anti-mycobacterial immune responses in TST-reactive household contacts

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Background: The tuberculin skin test (TST) is used to diagnose tuberculosis infection and guide preventive therapy prescription in household contacts of patients with tuberculosis. Sensitivity is limited by reduced reactivity in undernourished people at highest risk of developing disease. Micronutrient deficiencies are implicated in reduced TST reactivity as they are important determinants of anti-mycobacterial immunity. We previously demonstrated that topical zinc cream applied to TST augmented immune response sufficiently to improve diagnosis of tuberculosis infection. Because topical zinc is inconvenient, we investigated whether oral micronutrient supplementation augments TST indurations and improves diagnosis.

Methods: Between 2002 and 2006 we recruited 867 household contacts aged ≥ 15 years of 334 index cases with laboratory confirmed pulmonary tuberculosis. Each contact received one intradermal injection with tuberculin (0.5 IU in 0.1ml). Trained nurses read the resulting indurations after 48hrs. Participants were randomised to immediately receive either one dose of micronutrients (combined vitamin D 400 IU, vitamin A 5000 IU and zinc 25mg) or placebo. Indurations were re-read by nurses at 72hrs and the difference between the 72hr and 48hr indurations calculated.

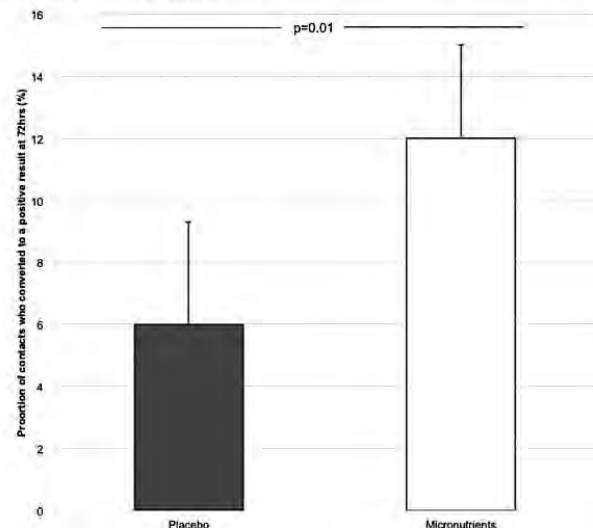
Results: The median induration at 48 h was 11mm. There was no difference in 48-72 h augmentation between the micronutrient and placebo groups (mean increase=0.68 vs 0.62; $P=0.6$). Among participants with an induration >10 mm at 48 h, micronutrient supplementation significantly augmented TST results at 72hrs compared to placebo (mean increase=0.71 versus 0.34, $P=0.05$). Using a threshold of ≥ 15 mm to diagnose TB infection, micronutrient supplementation significantly increased the odds of converting from a negative result at 48hrs to a positive result at 72hrs compared to placebo (odds ratio=2.2, 95%CI 1.2-4.0; $P=0.01$) (Figure).

Conclusion: In TST reactive individuals, one dose of micronutrient supplementation taken 48hrs after the initial tuberculin injection significantly augmented anti-mycobacterial immune responses and thus may

improve sensitivity of TST in undernourished household contacts.

Figure TST conversion and allocation

Figure: Proportion of contacts who converted from a negative TST result at 48hrs to a positive TST result at 72hrs according to allocation



PD-1020-29 Using country of origin to prioritize testing for latent tuberculosis infection in the United States

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Background: Testing and treatment for latent TB infection (LTBI) is an essential tool for reducing TB morbidity in low prevalence settings. However, given the large size of the foreign-born population in the United States, universal testing for LTBI may not be feasible. We sought to identify specific countries of origin that might be prioritized for LTBI testing based upon greater LTBI prevalence.

Methods: Using data from the U.S. National TB Surveillance System during 2005-2014, we analyzed reported TB cases among adults (≥ 15 years old). We used data from the U.S. National TB Genotyping Service to estimate the proportion of cases due to reactivation. The overall rate of reactivation was calculated from the number of reactivation cases and person years at risk, using population estimates from the American Community Survey and an overall foreign-born LTBI prevalence estimate from the 2011-2012 National Health and Nutrition Survey. LTBI prevalence by country of origin was estimated using the overall rate of progression and observed country of origin specific TB case rates.

Results: Among foreign-born adults, there were

65,045 reported TB cases; most cases (91%) were due to reactivation. The estimated annual rate of reactivation was 65 per 100 000 persons with LTBI (95% confidence interval [CI] 55-77). Ten countries of origin accounted for 71% of reactivation cases. Estimates of LTBI prevalence among the top 10 countries varied, with the highest LTBI prevalence among persons from Viet Nam (48% [CI 40-56%]) and Philippines (46% [CI 39-54%]), and the lowest LTBI prevalence estimates among persons from El Salvador (10% [CI 8-12%]) and Mexico (14% [12-17%]). The largest populations of foreign-born persons living with LTBI in the United States are from Mexico (1.7 million), Philippines (0.9 million), and India (0.7 million).

Conclusions: The majority of TB cases among foreign-born persons in the United States are due to reactivation of LTBI. TB elimination efforts need to balance addressing LTBI in foreign-born persons from countries with higher LTBI prevalence (e.g., Viet Nam and Philippines) and in foreign-born persons comprising the largest single population living with LTBI (i.e., Mexico-born persons).

PD-1021-29 Knowledge and attitudes about active and latent tuberculosis among index cases and contacts in three high TB burden Brazilian capitals

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Background: Close contacts are a target population for latent tuberculosis infection (LTBI) investigation and treatment because of their risk for progression to active disease. However, despite the high losses of contacts in all steps of investigation, most studies focus on treatment adherence. In this research, we explored knowledge and attitudes regarding TB transmission and prevention among index cases and contacts as part of a broader public health evaluation in Brazil.

Methods: A survey was conducted in twelve primary care units in Rio de Janeiro, Recife and Manaus, three cities with high TB incidence rates. Trained interviewers applied a standardized questionnaire on their knowledge and attitudes. Data on direct patients' costs were also gathered.

Results: Among 135 index cases, 91 (67%) knew they can spread TB, 94 (69%) feared for the health of their families and 119 (88%) would like their family to be evaluated for TB. Among 82 contacts, although 62 (76%) knew how TB is transmitted and its symptoms, only 23 (28%) knew how to prevent it. Sixty-one (75%) contacts declared they would take preventive therapy if prescribed, forty-six (56%) had not been investigated for LTBI or active TB; the main reasons were not believing they were sick (43%) and tests not being requested by the health team (35%). Among the 36 (44%) contacts who did undergo some investigation, evaluation for LTBI was performed in only 14 (39%). Their mean direct costs per visit were BRL 25.80 (USD 7.70). Most patients (78%) did not have any direct cost.

Conclusions: Contacts and index cases have positive attitudes towards TB prevention: patients fear transmitting the disease to their families and would like them to be investigated. Likewise, contacts would take medication to prevent TB if prescribed. These good attitudes towards TB prevention need to be exploited by TB programs. Costs for patients do not seem to be an important bottleneck. After discussion of these findings with local TB managers and health-care workers, solutions will be developed for evaluation by community-randomized trial.

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PD-1022-29 Programmatic implementation of the interferon-gamma release assay in Norway, 2009-2014

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Background: The incidence rate of tuberculosis (TB) in Norway is low, but high in risk groups. Mandatory screening for latent TB (LTBI) and TB disease applies to; (i) immigrants (IR birth-country $\geq 40/100\ 000$), (ii) occupational risk groups, and (iii) other groups at risk of TB. We review the implementation of QuantiFERON-TB Gold (QFT) as a confirmatory test in tuberculin skin test (TST) positive individuals.

Methods: Nationwide register-based study. Population: individuals tested with QFT 01.2009-06.2014 or who have been notified to the Norwegian Surveillance System for Infectious Diseases (MSIS) with TB or LTBI treatment 01.2009-12.2014. Data were linked through the national personal ID number on QFT-test results, TB-status (MSIS), demographic data (Statistics Norway), immunosuppressive treatment or disease (The Norwegian Prescription Database, Hospital Discharge Database). The requestor of the QFT-test was used to group individuals.

Results: The uptake of QFT has increased rapidly since 2009 with a total of 76307 QFT tests performed. Fifty-six percent ($n=42747$) of tests were in foreign-born. Primary health care and outpatient clinics were requestors of 71% of QFT tests, reflecting routine screening. Register-data were linked for 56645 individuals. Their QFT results (first if several) and TB status are presented in the Table. The mean follow-up time after QFT was 29 person-months (range 0-71, SD 19). The percentage with positive QFT result was higher in foreign-born than Norwegian-born individuals (42% vs 6%, RR 7.1, 95%CI 6.8-7.4, $P < 0.0001$). The percentage with LTBI treatment among QFT-positives (without TB disease) was low for all (20%), but higher in the Norwegian-born than the foreign-born group (24% vs 19%, RR 1.2, 95%CI 1.1-1.4, $P < 0.0001$).

Conclusions: The large discrepancy between the number QFT-positives and those who started LTBI treatment is of concern. Sub-group analyses may clarify whether this is related to test-indications, logistical challenges or poor acceptance of LTBI treatment.

Table Outcome of QuantiFERON-TB Gold (QFT) and TB status

Population	QFT positive n/N (%)	QFT inde- terminate n/N (%)	TB disease in QFT-pos ($n=12\ 042$) n/N (%)	LTBI treatment in QFT-pos without TB disease n/N (%)
Primary health care & outpatient clinics	9971/ 35 970 (28)	327/ 35 970 (1)	504/ 9971 (5)	1869/ 9467 (20)
Hospitalized internal medicine	1260/ 7879 (16)	486/ 7879 (6)	317/ 1260 (25)	93/ 943 (10)
DMARDs underlying disease	634/ 11647 (5)	284/ 11647 (2)	28/ 634 (4)	190/ 606 (31)
Other	177/ 1145 (15)	56/ 1145 (5)	18/ 177 (10)	26/ 159 (16)

PD-1023-29 Strong standard operating procedure: a key to effective implementation of isoniazid preventive therapy

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Background and challenges to implementation: Untreated latent TB infection can quickly progress to TB disease in people living with HIV. WHO recommends that PLHIV who are unlikely to have active TB should receive at least 6 months of IPT as part of a comprehensive package of HIV care. For a long time all PLHIV who have been screened negative for TB were supposed to be initiated on IPT; Although it was difficult to implement it due to many factors which include adherence to IPT, adverse drug reaction, shortage of medication and burden of pills. PASADA (Pastoral Activities and Services for people with AIDS

Dar-es-salaam Archdiocese) a faith based health services organization has managed to combat all this fear, although not in greater extent. This was successfully due to the introduction of strong standard operating procedures (SOPs).

Intervention: Every morning, health education is being provided. The information concerning IPT is being given to patients i.e. meaning, indication/contraindication, benefits and adverse reactions and what to be done when they get them. Adherence to medication is also emphasized. Then the patients will be screened for TB starting at the triage and also when she/he enters the doctor's room. If eligible, IPT is initiated after IPT counseling. All IPT patients' files are marked for easy identification and follow up every 1 month to monitor and minimize chances to miss the file so, the patient.

Results and lessons learnt: The patients who took IPT from august 2014 to February are 1309. There is an increase of almost 234 (18%) patients from November 2015 (1075) to February 2016. These 234 patients are still on IPT. Drop from IPT, are only 11 (0.84%), due to mainly adverse drug reaction. This shows how the interventions provide good results.

Conclusions and key recommendations: Through our IPT Standard Operating Procedures which we do follow daily, IPT implementation is easy and successful. If all TB-HIV centers will do the same they will have positive results like our center. TB disease burden will be reduced to a greater extent.

42. Infection control: knowledge and interventions

PD-1024-29 Prevalence of tuberculosis infection among health care workers and infection control in Nepal

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Background: Health care settings with inadequate Infection Control (IC) measures are at high risk of TB transmission among health care workers (HCWs) and other patients. The study measured prevalence of latent TB infection (LTBI) among health care workers (HCWs) and assessed IC infrastructures in health facilities in Kathmandu, Nepal.

Methods: A cross sectional survey was conducted in 28 randomly selected health facilities providing TB services in Kathmandu Valley. IC infrastructures (i.e. administrative measures, environmental controls and personal protective equipment) were assessed using a

checklist. 168 HCWs were Tuberculin tested using an international standard PPD 10 TU to measure the prevalence of LTBI and assessed for the risk factors with standard questionnaire. The associated variables were analysed by binary logistic regression model.

Results: Of 168 HCWs, 105 (62.5%) were female and 63 (37.5%) were male, and the mean age was 36.0 ± 9.9 (18-59) years. The prevalence of LTBI among HCWs was 56.5%. Increased age (OR 2.99, 95%CI 1.39 - 6.44), being employed in primary level of health facilities (OR 2.26, 95%CI 1.12 - 4.57) and exposure to TB patients for longer duration (OR 2.39, 95%CI 1.03 - 5.55) were independently associated with the risk of LTBI. The IC assessment showed that only 2 (7%) of the health facilities had written IC plan and 4 (14%) had IC focal person while none of them had TB specific IC plan. Few of them reported of HCW trained on TB IC (18%) and having provision of HCWs screening for TB (14%). Triage, separate waiting area, separate place for sputum production and mechanical ventilation were lacking in majority of the facilities. Use of respirators was minimal provided inadequate availability of N95 masks for HCWs and lack of surgical masks for TB patients.

Conclusions: The study showed high prevalence of LTBI among HCWs and IC infrastructures seems to be inadequate in the health facilities. Regular screening of HCWs for TB needs high consideration. Strengthened and cost effective IC measures including effective use of respirators are recommended.

PD-1025-29 Infection control in tuberculosis hospitals in Almaty, Kazakhstan: knowledge, practices and infrastructure assessment, 2015

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Background: Kazakhstan is one of the world's high multi-drug-resistant tuberculosis (MDR-TB) burden countries. In 2011, the country introduced national annual TB infection control (IC) training. We studied the subsequent IC-related knowledge and practices of health-care workers (HCWs) and evaluated the implementation of IC practices in TB facilities in the major city in Kazakhstan.

Methods: We conducted a cross-sectional study in five facilities providing in-patient treatment for TB in Almaty City and Oblast in August 2015. An

interviewer-administered questionnaire covered sections on knowledge, and practice including clinical features, transmission, MDR-TB, ventilation and personal protective equipment (PPE). We graded knowledge using a 10-point score based upon answers to a composite of questions; a score of ≤ 4 was considered to be poor knowledge. We used logistic regression to identify factors associated with practice of HCWs towards TB IC. Prior to interview, practices of interviewees were observed and, subsequently, unannounced visits assessed the implementation of IC in the facilities.

Results: Of the 724 HCWs interviewed, 68 (9%) had never attended TB IC trainings. Interviewees had very good knowledge about clinical aspects of TB but poor knowledge was identified in: transmission of TB (15%), MDR-TB (15%), ventilation (11%), and PPE (17%). Observation, however, showed 470 (65%) and 69 (10%) of HCWs misused mechanical room ventilation and PPE, respectively. Overall, only 41% of HCWs with excellent knowledge on TB transmission demonstrated proper practices of IC. Unannounced visits showed stock-outs of respirators, and non-functioning mechanical room ventilation in all facilities. Non-attendance at IC trainings was associated with poor self-screening of HCWs for TB and HIV (aOR=3.7, 95%CI 2.0-6.9); while those with more years of education more likely complied with annual self-screening (aOR=0.4, 95%CI 0.2-0.9) and properly practiced protection by ventilation (aOR=0.1, 95%CI 0.1-0.2).

Conclusions: Despite annual IC training and good TB knowledge, a substantial proportion of HCWs have inadequate IC knowledge and poor practices, while PPE is not always available and room ventilation to prevent transmission of TB is often not functioning. Hospital administrators should ensure appropriate safety equipment is always available and functioning, and demand adherence of HCWs to IC preventive measures.

PD-1026-29 Tuberculosis infection control knowledge, attitudes and practices of health care workers in primary health care facilities in Mangaung Metropolitan, South Africa

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Background: Tuberculosis (TB) infection control within healthcare facilities is a key strategy in preventing the spread of TB. In high TB-HIV-burden contexts such as South Africa, TB is easily transmitted to healthcare workers (HCWs) and patients, particularly to those who are immunocompromised. It is therefore vital that HCWs meticulously apply the established infection control measures to safeguard

themselves and their patients. The aim of this research was to assess TB infection control-related knowledge, attitudes and practices among HCWs in primary healthcare (PHC) facilities in Mangaung Metropolitan (Free State Province).

Methods: A cross-sectional survey of HCWs' TB infection control knowledge, attitudes and practices was conducted in November 2015. Nurses and facility-based community healthcare workers (CHWs) across 40 facilities in Mangaung Metropolitan were invited to participate in the study. A total of 202 nurses and 34 CHWs completed self-administered questionnaires. The data was subjected to univariate and multivariate analysis using SPSS 23.

Results: More than half of the respondents ($n=118$; 51.8%) had received TB-HIV-related training during the year preceding data collection. Despite a high average score of 72% on knowledge of TB infection control, 27.1% ($n=60$) of HCWs nevertheless revealed poor TB infection control practices, including not always using an N95 respirator when collecting sputum ($n=123$; 54%); not always isolating presumptive TB patients from other patients ($n=125$; 54%); and not always providing coughing patients with tissues/masks ($n=86$; 37%). The majority of respondents ($n=198$; 85%) were afraid of contracting TB at work. Results showed that sound knowledge of TB prevention and fear of TB infection at work significantly predicted good infection control practices [$F(2, 217) = 9.42, P < 0.05$]. Knowledge of TB ($t=3.575; P < 0.001$) made a statistically unique contribution to the prediction.

Conclusion: Despite continuous policy developments and consistent training efforts, PHC-level HCWs in Mangaung Metropolitan remain inadequately equipped to prevent TB by means of proper infection control. Knowledge about TB infection control and fear of acquiring TB at work significantly influenced TB infection control practices, suggesting a need for alternative efforts towards capacitating HCWs in TB prevention in PHC facilities. Interventions should thus purposefully steer towards remedying the identified deficiencies.

PD-1027-29 Improved ventilation for the cessation of tuberculosis transmission: an outbreak on a college campus, 2010-2013, Taipei, Taiwan

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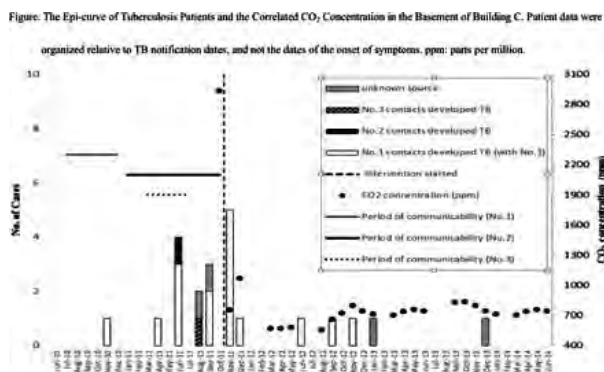
Background: It is difficult to quantify the influence of improved ventilation on the control of TB transmission. A smear-positive index TB patient at College A reported to the TB Registry in late November, 2010. He took classes in a basement of building C, comprised of 17 classrooms on 3 underground floors with a CO₂ concentration of 2936 parts per million (ppm).

Methods: All students or employees at College A that developed active TB during 2010-2013 were investigated by public health authorities. An outbreak committee organized in October, 2011 suggested immediately increasing ventilation in Building C's basement; decreasing the density of students in classrooms; encouraging natural ventilation by opening windows and doors. In December, 2011, the committee further suggested the removal of two-thirds of the un-openable stained glass windows located above the front-door on the first floor and shut down the 17 classrooms. CO₂ concentration, as an assessment of ventilation, was measured serially in the basement of building C. Secondary attack rates of contacts were analyzed before and after building-reconstruction.

Results: A total of 22 TB patients were identified in this outbreak including the index patients. Chest radiograph screenings for 1,006 students and teachers were done and 159 close contacts received isoniazid preventive therapy. Excluding 4 contacts whose index patients could not be identified (Figure), the secondary attack rate dropped significantly after ventilation was improved (17/673 vs. 0/333, $P < 0.001$, Fisher's Exact test). To exclude the possibility that LTBI treatment caused the drop in secondary attack rate, we further used the date of commencement of treatment as a censored date for those who received LTBI treatment. The secondary attack rate calculated with denominators of person-days still dropped significantly (17/507805 vs. 0/136942, $P=0.032$, χ^2 test).

Conclusions: Besides contact investigations and targeted LTBI diagnosis and treatment, environmental control should be emphasized. It is crucial to identify environmental control defects and to make improvements in ventilation even when reconstruction is necessary.

Figure The Epi-curve



PD-1028-29 Tuberculose en milieu de soins au Sénégal

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Problématique : Le risque de transmission de *Mycobacterium tuberculosis* dans les établissements sanitaires est réel. L'application de mesures de lutte contre l'infection tuberculeuse et la surveillance régulière de la tuberculose-maladie chez les personnels de santé et à tous les niveaux du système sanitaire constituent une priorité de santé publique, non seulement pour le personnel sanitaire et administratif, mais aussi pour l'ensemble des usagers.

Objectifs : Faire l'état des lieux de l'infection tuberculeuse chez le personnel de santé et évaluer les mesures de lutte contre l'infection mises en œuvre dans les structures sanitaires du Sénégal.

Méthode : Un questionnaire renseignant sur les cas déclarés de tuberculose chez le personnel de santé entre 2010 à 2014 a été diffusé dans tous les établissements sanitaires.

Résultats : 77 cas de tuberculose ont été enregistrés, soit un taux annuel moyen de 15,4 cas. Les hommes représentent 59, 7 %. L'âge moyen est de 40,6 [20, 71]. L'incidence annuelle est de 214,4/100 000 agents en 2010. La région de Dakar est plus touchée avec 57 % des cas et principalement les services de pneumologie et Maladies infectieuses et tropicales du Centre Hospitalier Universitaire National de Fann qui ont notifié 18, 2 %. Les infirmiers sont majoritaires (41,5%) suivis du personnel de soutien (23%) et des médecins. C'était essentiellement des TPM+ (52,3%). un cas de TB MR a été enregistré en 2014 et trois cas étaient VIH1.. Un CLIN a été mis en place dans toutes les structures enquêtées mais le plan de lutte adopté n'a été exécuté que dans 25% des établissements sans aucune évaluation durant ces cinq années.

Conclusion : La tuberculose chez le personnel est sous évaluée mais reste plus fréquente dans les services prenant en charge les malade en hospitalisation. Malgré la mise en place de CLIN, l'exécution des plan de lutte élaborés est freinée par la rareté des ressources financières. L'émergence de forme multi résistante et ultra résistante constituent une menace certaine pour tous les usagers de nos structures sanitaires..

PD-1029-29 Enhanced infection control program among health staff in tuberculosis services during the Ebola epidemic in Conakry, Guinea

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Background: The 2014-2015 largest and sustained Ebola epidemic provoked deaths among health staff in Guinea. In order to prevent Ebola infection and deaths among health staff working at Tuberculosis services, the National Tuberculosis Program (NTP) and Damien Foundation (Belgian Non-Governmental Organization) implemented an enhanced infection control program.

Methods: From April 2014 to December 2015 this cohort study included health staff (medical doctors and nurses) working in Tuberculosis services of health facilities in Conakry. The infection control program included: 1. A knowledge, attitude and practice (KAP) infection prevention survey among health staff. 2. An infection prevention training taking into account results of KAP survey. 3. Provision of consumables for infection prevention and supervisions on a monthly basis. The number of infection and Ebola related deaths among health staff was monitored.

Results: The KAP survey included: 61 health staff working at tuberculosis services of 18 health facilities. 36 (59%) were nurses. The age mean was 39 years (Interquartile Range=IQR 29-48). 34 were female (57%). 49 (80%) had less than five years of tuberculosis working experience. Concerning tuberculosis training: 14 (23%) were not trained; 34 (56%) had ≤ five training sessions and 13 (21%) had ≥ six training sessions. Concerning infection prevention: 48 (78%) were not trained; 37 (66%) acknowledged to wash their hands before physical examination of patients. The infection prevention training included 26 health staff (selection criteria was at least one representative of the 18 health facilities), where 13 were nurses (61%); 14 (54%) were female; the age

mean was 38.5 (IQR 31-50) and 19 (73%) were not trained on infection control. After training, supervision and infection provision of consumables for infection prevention were performed on monthly basis, no stock outs were notified. No infection or deaths related to Ebola among health staff were notified at Tuberculosis services during the study period.

Conclusions: An infection control program was developed using the results of a KAP survey about infection prevention among health staff. Support to health staff by provision of infection prevention consumables and close supervision were important to avoid infection and deaths related to Ebola among health staff in Conakry, Guinea.

PD-1030-29 Involvement of community volunteers in Chisokone Market congregate setting (hot spot), Copperbelt Province, Zambia

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Background and challenges to implementation: In 2007, Zambia developed a national TB infection control (TB IC) strategy that included among many strategies; Capacity building in TB Infection Control (TB IC) at all levels of health care service delivery to prevent the spread of *Mycobacterium tuberculosis*.

One such congregate setting is Chisokone Market in Kitwe Zambia, a sprawling makeshift market catering for both local and foreign traders who besides trading, too spend nights at the premises alongside homeless street kids - both being vulnerable to respiratory infection, TB inclusive.

Intervention or response: One committed community volunteer (TB treatment supporter) was identified and trained in a five (5) day long TB IC programme and entrusted with responsibility to identify clients (traders & street kids) with signs of TB. She would bring them to diagnostic health facilities for physical examination and sputum screening, collects drugs for those diagnosed with TB and observe them swallow the drugs at the market as well as bring those for review and due for sputum follow ups.

Results and lessons learnt: Since introduction of program at the market in 2010, patients with Pulmonary bacteriologically confirmed TB has reduced from sixteen (16) to nine, in 2015 due to early detection and treatment. Also record was reduced number of lost to follow up as well as the reduction in mortality by over 75% over the same period.

Conclusion: The market initiative is good for the TB program and TBIC in particular, though many are challenges such as, volunteer being over whelmed

with work ,she needs to re-visit health facility 2 - 3 times in a week to collect drugs or transport sputum while leaving her mechanize unattended to. Another challenge is transport costs borne by the volunteer and; most patients having no permanent places (Depos) were they would stay and sleep.

Recommendations: Identify and train more volunteers from the market, draw up a program of sensitization in form of focus group discussions, drama performance or public address system plus radio listening programs. Identify a place where sputum from presumptive cases could be kept and collected by currier to diagnostic centre.

PD-1031-29 Clinical characteristics and delay among patients diagnosed with pulmonary tuberculosis after hospitalization

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Background and challenges to implementation: Delay in diagnosis of pulmonary tuberculosis (pTB) is epidemiologically significant problem among all healthcare settings. Since many hospitalized patients have weakened immune systems, delayed diagnosis of pTB may result in outbreaks and involve higher medical costs. However, diagnosis of pTB is difficult because patients often present atypical manifestation. In this study, we identified the risk factors of delay in diagnosis of pTB.

Intervention or response: In this single center study, 40 patients diagnosed as pTB after hospitalization in National Center of Global Health and Medicine, Japan, between January 2011 and December 2015 were reviewed. All patients were diagnosed as either possible pTB or other diseases, and later diagnosed as pTB during the hospitalization with positive result in at least one of the following: sputum smear, sputum culture, or Tb-PCR. The primary outcome is to elucidate the risk factors of delay in diagnosis of pTB and the clinical characteristic among pTB patients diagnosed after admission.

Results and lessons learnt: In the 40 patients diagnosed as pTB during their admission, 31 of 40 (77.5%) were male with the median age was 75.0 years old (IQR:61.3-86.3), 12 patients (30.0%) showed poor performance status on admission. Most of the initial diagnosis at admission was pneumonia ($n=14$; 35.0%), the most frequent underlying medical condition were diabetes ($n=15$; 37.5%). Symptoms on admission were cough ($n=26$; 65.0%), persisting fever ($n=19$; 47.5%), respiratory failure ($n=18$; 45.0%), weight loss ($n=16$; 40.0%), and night sweat ($n=12$; 30.0%). The median duration between

admission and the diagnosis of pTB was 15 days (IQR:4.0-23.5). Thirty-nine patients (97.5%) presented abnormal findings of the chest X-ray on admission. Sputum smear, culture, or Tb-PCR were positive in 42.5%, 50.0% and 7.5% of the patients, respectively. Nine patients (22.5%) died.

Conclusions and key recommendations: More than half of the patients yielded positive-culture negative-smear. It is difficult to diagnose pTB by early with relatively low percentage of positive smear. We need further study and protocol for a better diagnosis of pTB in the early days in healthcare settings.

PD-1032-29 Contribution of health facility patient triaging to the case detection trend in 15 provinces of Afghanistan

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Background: At health facilities (HFs) Tuberculosis (TB) patients were not identified, separated and fast tracked to increase case detection and minimize exposure to others. To improve these indicators National TB Program (NTP) has been working to implement TB infection control (TB IC) measures at 205 HFs of 15 provinces with support from Challenge TB (CTB) project.

Intervention: CTB helped the NTP to implement TB IC measures at HFs by health staff through on the job training where health staff took to the DOTs learning centers to practically assess the HFs buildings design, TB transmission, patient flow, clients triage for TB, recording and reporting and to copy the best practices. Also disseminated 3000 copies TB IC pocket guide and laboratory biosafety manual, disseminated 26000 job aids, redesigned 190 HFs , collected and analyzed data to monitor progress. In 2016, CTB and NTP conducted an assessment to determine if the HFs triage system had contributed to improved TB suspect identification, testing and case detection. We analyzed the data recorded between 2014 and 2015 at 103 of the 205 HFs where they had implemented TB triaging activities.

Results: The study revealed that from 2014 to 2015, the number of TB suspect identified at the 103 HFs increased by 109% (from 61259 in 2014 to 66482 in 2015). Among those identified suspect, the number tested for TB increased by 108% (from 59662 in 2014 to 64277 in 2015). Similarly the number of new sputum smear positive TB cases increased by 120 % (from 4376 in 2014 to 5245 in 2015).

Conclusions: The study determine that TB IC

activities, mainly triage contributed to improved suspect identification and case detection in TB IC covered HFs. These TB IC control measures should be maintained in 205 HFs and expanded to additional HFs to further improve TB control in Afghanistan

Table Contribution of triage by HFs to case detection

Variables/Year	2014 n (%)	2015 n (%)	% change (2014-2015)
HFs covered by TB IC	103 (29)	103 (29)	
TB suspects identified	61 259	66 482	109%
TB suspects tested	59 662	64 277	108%
New sputum smear positive cases notified	4376	5245	120%

PD-1033-29 Impact of TB infection control on patient waiting time and early diagnosis at health facilities in 15 provinces of Afghanistan

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Background: People who work or receive care in health care settings are at higher risk of M. Tuberculosis infection. Therefore Challenge TB (CTB) project assisted National TB Program (NTP) to implement Tuberculosis (TB) infection control (IC) measures at health facilities (HFs). In 2015 an assessment conducted in 45 HFs of 11 provinces to determine the impact of TB IC on patient waiting time from his/her arrival to departure and treatment initiation.

Intervention: Challenge TB helped NTP to train front line health staff on TB IC measures, assess risk of TB transmission within HFs, establish TB IC committee at HFs, develop TB IC pocket guide, develop TB IC job aids, redesign HFs to consider TB IC measures, establish well ventilated sputum collection areas, collect and analyze data to monitor progress and provide feedback. We selected convenient samples of 230 (intervention =158, control=72) interviews of suspect TB cases from 45 intervention and control health facilities of 11 provinces. We utilized questionnaire, documented patients arrival time, detection as suspect, sputum collection time, and diagnosis and treatment initiation.

Results: As concluded from the data that in intervention HFs, mean suspect identification time from his/her arrival was 35 minutes and their departure was 75.7 minutes. Also mean sputum collection of three samples took 32 hours and time to diagnosis to treatment initiation was 40 hours. Contrary in control HFs, mean suspect identification time was 62 minutes and their departure were 182 minutes, mean sputum collection time was 65 hours and diagnosis and treatment initiation was 72.3 hours.

Conclusions: The study revealed that time interval of TB suspect identification from his/her arrival to departure and from diagnosis to treatment initiation was significantly low in intervention HF, therefore TB IC control measures enhancement and implementation is recommended in all similar settings.

Table TB suspect arrival time

Table: TB suspect arrival and departure time in intervention and control health facilities (HFs)

Indicators	Intervention HFs	Control HFs
Sample size	108	72
TB suspect detected time	35.1 Minutes	62 minutes
suspect departed time after first sample collection	75.7 Minutes	182 Minutes
sputum sample collected at least three from detected suspect	32 Hours	65 Hours
Required time by lab to process sputum for microscopy	48.2 Minutes	69.6 Minutes
Required time by smear Microscopy and record & reporting	30 Minutes	56 Minutes
Time to report result by lab to DDTs clinicians	40 Hours	69.5 Hours
Time from diagnosis to starting treatment	40 Hours	72.3 Hours

PD-1034-29 Effectiveness of tuberculosis infection control committees on implementation of TB Infection control measures at health facilities in Afghanistan

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Background: People who work or receive care in health care settings are at higher risk M. Tuberculosis infection. Therefore, Challenge TB (CTB) project assisted National Tuberculosis Program (NTP) to implement TB infection control (TB IC) measures at 205 health facilities (HFs) by TB IC committees in 15 provinces. In 2015, an assessment conducted in HFs in 9 provinces to determine the effects of this approach on implementation of TB IC measures at HFs.

Intervention: CTB assisted NTP to establish TB IC committees at HFs, integrate TB IC plan into general infection prevention plan, develop TB IC pocket guide, develop Job aids, redesign HFs and train staff. We assessed 135 (34%), (90 (44%) from intervention and 45 from control) of 400 HFs, using a data collection tool. We evaluated each facility's managerial, administrative, environmental, and personal protective controls through observation and interview with committees' members, review of charts and air flow within the rooms.

Results: The intervention HFs implemented 87.5% of the 7 TB IC standards, while control HFs met only 5% of them. For example, 100% of intervention HFs had a TB IC plan; 95% redesigned, 100% had sputum collection area, 75% implemented cough triage of clients, 76% of both suspected and confirmed TB patients used face mask and 90% of HFs separated patients and 77% had cough etiquette measure implementation. Contrary, in control facilities, 0% had TBIC plan, 10% redesigned, 5% had sputum collection area, 6% implemented cough triage, 7% of suspect and confirmed TB patients used mask. Also, only 2% of patients were separated and 5% implemented cough etiquette.

Conclusions: The TB IC committees played an important role in promoting TB IC standards that ultimately made working environment safer for staffs, clients and communities. Thus, we recommend it as a priority action at HFs and other similar settings.

TB IC standard status in intervention and control HFs

Variables	HFs with TB IC Interventions 2015	HFs without TB IC interventions 2015
Sample size	90	45
Existing TB IC plan	100%	0%
Sputum collection area	100%	5%
Redesigning HFs	95%	10%
Cough triage	75%	6%
Patient Separation	90%	2%
Cough etiquette	77%	5%
Face Mask used by patients	76%	7%

43. Media engagement in TB interventions

PD-1035-29 Measuring community contributions to the TB Programme using simple RR forms and methods in 12 districts, Indonesia, 2015

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Background: The Indonesian Association Against TB (known as PPTI) is a CSO established since 1968. One of the activities is to empower community in participating to control TB. There are a lot of community workers (cadres) were trained to identify and support TB patient without recording and

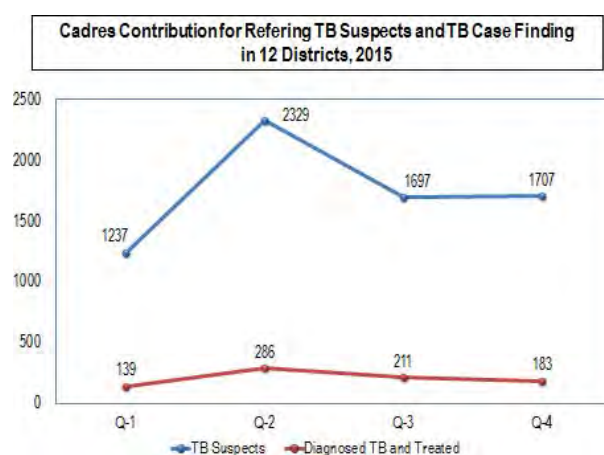
reporting system to evaluate their contribution. The project is in 12 districts of 8 Provinces funded by The Global Fund component TB SSF phase 2 year 2014 - 2015.

Intervention: Developed 'simple' RR system for TB cadres. Trained 478 cadres to record and report using TB Cadres Forms. PPTI provided the forms and reward for cadre's achievement in referring TB suspects to health centers and monitor TB treatment until complete. Cadres should collaborate with health centers to have approval and send the forms to PPTI HQ every month.

Results and lessons learn: 6.970 TB suspects were found and referred to health centers by cadres; 819 were diagnosed as TB patients and got treatment; 216 TB patients among those who got treatment, have cured (the rest of it still in process). All data have been validated and cross checked during a monitoring meeting of cadres. There are 42 invalid forms (0,5%) due incomplete in filling data or not being verified by health centers. Uncompleted forms send back to cadres to be corrected. Cadres contribution increase after supervision and monitoring meeting.

Conclusions: TB program should have standardized RR system for CSO to measure community contributions. The Form should be simple and easy to fill. Close supervision and monitoring is needed to improve the performance of cadres and it should be validated by health centers. This project proves that community has a direct role in TB control and not only to educate people about TB but also to identify TB suspects and ensure the treatment done and cured.

Figure Cadres contributions



PD-1036-29 #UnmaskStigma: a global advocacy initiative to address TB stigma

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Background: South Africa has the third-highest tuberculosis incidence rate in the world with a high HIV-TB co-infection rate and a large drug-resistant TB burden. Despite mounting evidence of stigma driving diagnostic delays and treatment interruptions, few interventions have attempted to reduce TB-related stigma directly.

Intervention: The Global #UnmaskStigma Initiative, conceived by TB survivors and activists, aims to reduce TB-stigma by engaging the public through the sharing of personal stories, education and social mobilization. From 2014 to 2015, four concerted #UnmaskStigma Campaigns and 52 educational sessions targeted the public, healthcare workers and students with information on prevention and healthcare seeking practices. TB patients wear masks to protect others. Approximately 35 000 people 'unmasked stigma' by wearing masks in public and posting pictures of solidarity on social media, resulting in a cumulative on-line reach of ~52 600.

Lessons learned: #UnmaskStigma received broad support from stakeholders from 17 countries, including Members of Parliament, policy makers, media personalities, TB-HIV survivors and advocates. 14 advocacy partners, 7 universities and 12 healthcare facilities distributed 34720 masks, 23040 stickers, 9360 pamphlets, 150 posters and several survivor short-films featuring stigma reduction messaging. Prominent print, radio and television coverage increased exposure significantly, although exact figures were challenging to estimate. Numerous people affected by these diseases have subsequently come forward to access care and participate: 'After surviving XDR-TB I want to create awareness and help others.' Focused qualitative evaluations are recommended to describe the relative contributions of complementary components.

Conclusions: Our experience shows that society is ready to acknowledge the harmful effects of TB-HIV stigma and is willing to take part in large acts of solidarity. Social media linked to mainstream media and educational activities can enhance grass-roots advocacy to transform public perceptions. Further research is needed to understand how participation translates into real reductions in stigma.

PD-1037-29 Does mobile technology improve referrals and reduce delay in diagnosis and treatment initiation of TB patients? Impact analysis from India

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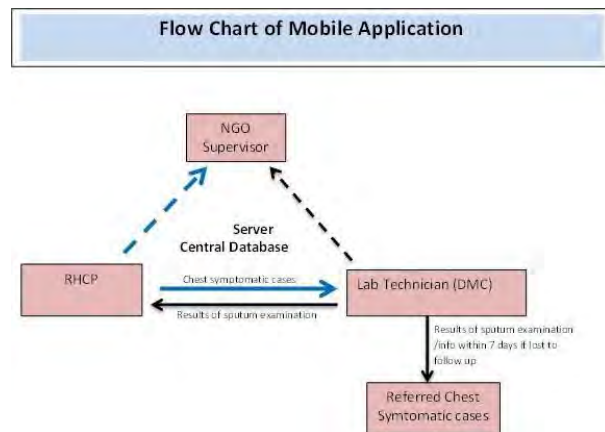
Background and challenges to implementation: In accordance with pillars of post 2015 global Tuberculosis strategy of WHO - Integrated patient centred care & prevention (early diagnosis & treatment), bold policies & supportive systems (engagement of private providers) and intensified research & innovation (promote innovations), Rural health care providers (RHCPs) 'first point of contact' for curative services in remote geographic areas in India were trained on TB and use mobile application to refer presumptive TB patients. Objective is to demonstrate effectiveness of mobile technology for real time referrals, early diagnosis & treatment initiation of TB patients in a tribal district.

Intervention or response: Two inter-operable applications were developed. One application was used by 25 RHCPs and other by 3 LTs. 64 RHCPs referred through non-mobile. Mobile application developed is easily customizable, tracks referrals & creates real-time central database. The application is being piloted in three blocks of Khunti, tribal district in India.

Results and lessons learned: About 56% ($n=108$) of diagnosed TB patients were diagnosed within 1 day of referral through mobile compared to 34% ($n=65$) through non-mobile. 56% ($n=105$) were initiated on treatment within 7 days of diagnosis whereas 34% ($n=67$) through non-mobile. Successful referrals per RHCP through mobile were 43 & 8 through non-mobile. 5 TB patients were diagnosed per RHCP through mobile & 1 through non-mobile. However few challenges were faced in maintenance of android phones.

Conclusions: Mobile technology increases referrals, early diagnosis & treatment initiation of TB patients. Targeted intervention in tribal district is benefited by mobile application.

Figure Flow chart of mobile application



PD-1038-29 How do the media see tuberculosis in India?

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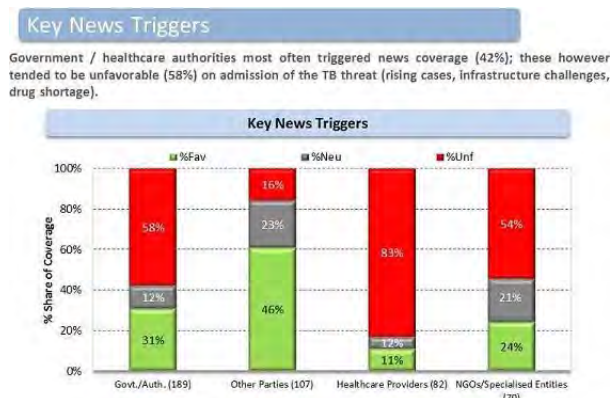
Background: The media can play a key role in creating awareness about TB as a significant public health concern, placing TB on the national health and development agenda and lobbying policy makers to develop relevant policy interventions. The media content analysis is conducted with the objective to understand how media covers TB.

Methods: A total of 1,029 articles from diverse English and Hindi media sources- national and regional editions were identified during April-September 2013. These were further shortlisted to 448 based on relevance, with only articles of concrete discussion/indication about TB and not just a passing, incidental mention. A favorability rating system was designed using a (0- 100) scale based on placement, message and tone of voice.

Results: 52% articles were rated unfavorable due to coverage on infrastructure challenges, rise in new cases/death toll and shortage of essential TB drugs. 75% coverage featured TB in headline mostly in english dailies (90%). 92% coverage was in the form of 'news' items. Negative messages prevail well ahead of positive sentiments. The key news triggers and the trending topics in TB have been detailed in Figures 1 and 2. Government running effective programs to treat & cure TB and innovation/R&D were the key positive messages noted.

Conclusions: Health care providers are important opinion drivers and therefore, should be kept informed of the developments in this area. Regular media sensitization on TB, preparation of media toolkit (TB) and a dedicated media cell in National TB Programs are recommended.

Figure Key news triggers



PD-1039-29 Trends in media coverage of TB: a retrospective analysis

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Background: Despite TB being curable, it still accounts for 2.2 million deaths in India (WHO Global TB Report 2015). A TB-Free India is possible only with wider engagement of all stakeholders, including media. Media, if engaged effectively can contribute significantly by raising public awareness on TB and capturing gaps that need to be addressed through Government and stakeholder action.

Methods: This study analysed the trends in media coverage of TB to understand the kind of media engagement that has happened in the past year and decide media engagement strategy for the Call to Action. Online media reports (English) (Jan 01, 2015 - Dec 28, 2015) and print media reports (Oct 01, 2015-Dec 26, 2015) were analysed retrospectively using select keywords. A total of 1404 English reports were analysed (1321: online; 83: print). Additionally, detailed bivariate analysis was carried out by placement, publication, writers, type of report, region, issues highlighted and quotes carried.

Results: Majority of online coverage was in sync with launch of key reports (WHO global TB report 2015), launch of projects (Mission TB-Free Haryana), announcements from government/ ministry, stakeholder engagement consultations (Consultation with parliamentarians), World TB Day, and engagement of public figures like Amitabh Bachchan, Richard Verma and Ratan Tata. Reports of PTI and ANS were later reported by other online portals, followed by reports related to launch of 'TB-free India' program and toll-free helpline in April 2015. Spike of high reporting was found in March, September and December 2015, coinciding with specific engagement

of celebrities and launch events. Various topics were covered, such as issue of access and care, patient stories, under reporting of cases, availability of medicines, X/MDR-TB etc. Types of reports were largely news articles mostly on report launches. In print, there were few feature articles and Op-Eds along with interviews of patients and TB survivors.

Conclusions: TB has been extensively covered by media and the buzz is higher during events such as World TB Day & launch of Annual Reports only. For a TB-Free India, voices of patients, celebrity action and policy gaps need to be highlighted through more Op-Ed pieces by experts /celebrities.

PD-1040-29 Is more better? A descriptive study comparing two hashtags

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Background: Although there are traditional means to disseminate information, the advent of internet and social media (SM) has revolutionized communication. In a short time period, advocacy and communication within the HIV epidemic has proven instrumental in increasing funding and raising awareness of the disease. With increased use of SM, this new era creates infinite potential in promoting awareness. Our study aims to understand if there is a relationship between funding allocation and social media advocacy.

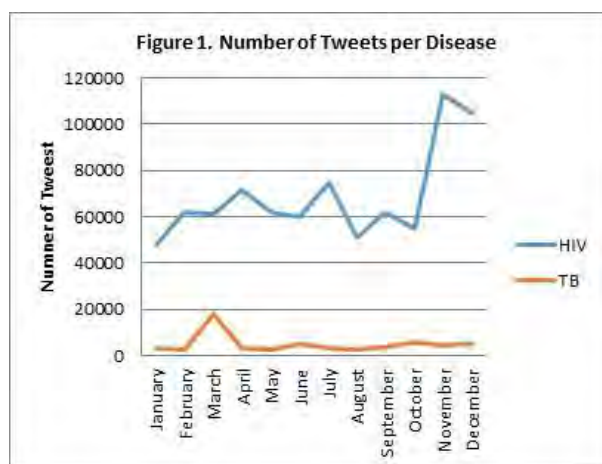
Methods: We utilized Twitter as a SM platform. Twitter allows users to post 'tweets' which are messages limited to 140 characters. Tweets allow users to post hashtags (#) with a topic next to the hashtag (e.g. #tuberculosis). Searches can be completed for specific hashtags to enumerate the number of related tweets, and the number of participants following. Utilizing Symplur, a website that collects information on healthcare based hashtags, we compared #tuberculosis and #HIV from 01/01/2015-12/31/2015. For these hashtags, we searched the number of tweets per month and the number of participants tweeting. We then analyzed the data and created graphs using Excel.

Results: From Jan 2015-Dec 2015, we identified 825,195 #HIV tweets compared to 59,534 #tuberculosis tweets. Hence, twitter users were 13 times more likely to tweet about HIV than TB. This translated into an estimated 26,864 twitter users tweeting #HIV per month compared to 2,960 twitter users tweeting #tuberculosis. Hence, the #HIV had 9 times more participants on average monthly when compared to #tuberculosis. In 2016, the Global Fund has allocated 3 times more funding towards HIV than TB and US Foreign Assistance funding has allocated

29 times greater funding for HIV/AIDS (5.76 billion dollars) than TB (195 million dollars).

Conclusions: Our study suggests that Twitter posts frequency and funding allocation may be associated. Further, we highlight a tremendous missed opportunity for TB advocacy that could potentially improve TB funding allocation. Social media has great advocacy potential and could play an important role to strengthen the voice of TB. Data on message timing, ideal SM platform, and message quality should inform these efforts to maximize impact.

Figure Number of tweets per disease



PD-1041-29 School children as 'TB soldiers': astounding results of pilot intervention in schools in two districts in Rajasthan, India

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Background: Sensitization of adolescents and older children can bring about a positive change by increasing community participation and ownership towards TB control. Realizing their value as social change agents, MAMTA, through Project Axshya, decided to engage them in TB control. A school-based intervention was conceived and designed wherein school students were sensitized on TB control and groomed as 'TB Soldiers'. In this study, this intervention is being evaluated in 2 districts of state of Rajasthan, India: Tonk and Sawai Madhopur (~2 million population), where it was rolled out on pilot basis.

Intervention: Mapping was done to identify schools where children from vulnerable and marginalized population study. A well-structured communication protocol was developed to sensitize children grooming them as 'TB-Soldiers'. Principals of selected

schools were requested for '15 minute slot' during Morning Prayer. During September-December, 2015, District Coordinator (DC) of Axshya conducted interactive communication exercise with students (Grade 6-12). Three key messages were delivered: TB is communicable and its transmission must stop to protect society, signs and symptoms of TB, whom to inform if they know any presumptive TB patient (PTB). A teacher volunteering as focal point ('Axshya Prerak'), informed DC about PTBs reported by children. The children identifying PTBs were felicitated as 'TB Soldiers' at the school.

Results: 100% of approached schools participated. Activity was conducted in 18 schools involving 3500 students (Grades 6-12). 134 PTB were reported by students to 'Axshya Prerak'. On examination, 32 of them were diagnosed as New Smear Positive TB cases. This implies 24% specificity in case identification by students. Most PTBs were identified by students of Grades 10 and 11. 25% cases were reported on same day as sensitization and another 33% within 2 days. 40% PTBs lived in neighborhood of students while 60% were from different locality. Only cost incurred was 18 man-days of DC and \$206 paid to community volunteers for transporting sputum.

Conclusions: Piloted 'School-Intervention provides a highly-effective ultra-low cost model for TB control with benefits reaching beyond family and neighborhood of sensitized children. Unutilized till now, sensitizing and engaging school-children as 'TB-soldiers' holds immense potential and is strongly recommended for upscaling.

PD-1042-29 Schoolchildren raise tuberculosis awareness among their peers

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Background and challenges to implementation: To spread tuberculosis (TB) information among school children, the City Health Office (CHO) of Gingoog (population: 127,906) in Misamis Occidental, Philippines, engaged and oriented on TB top five Grades 5 to 8 pupils (11-14 years old) from three private and three public schools. Three years prior to engaging the pupils, the CHO had screened only 28 children with presumptive TB in 2010, 20 in 2011, and 16 in 2012. All the children tested positive and were treated; however, the number of children screened was not improving.

Interventions or response: With the consent of the schools and concerned parents, Gingoog CHO oriented about 50 top pupils on TB and its cause, transmission, symptoms, prevention, and cure. The orientation also corrected misconceptions on TB; for

instance, that it is hereditary. Those who completed the briefing were given the title *Kiddie TB Patrollers*. In poster-making and slogan-writing contests, the Patrollers translated TB information into messages for their peers. They conducted a room-to-room campaign to urge their classmates to see their teacher or school clinic for proper referral should they experience cough of two weeks or more. They also shared TB information with family members. TB quiz winners were chosen to replace those who had graduated. With USAID technical assistance, Gingoog CHO provided the Patrollers with referral slips, trained them on recording and documentation of referrals, and supported their Lung Month activities. **Results and lessons learnt:** Kiddie TB Patrollers referred about a third of all children who underwent tuberculin skin testing in 2014 (20/51 or 39%) and 2015 (31/101 or 31%). Of the children diagnosed with TB, 14 (56%) of 25 cases in 2014, and 26 (90%) of 29 cases in 2015 were attributed to the Patrollers' referral. While the use of the referral slip, which started late in 2015, was something the Patrollers have yet to get used to, the CHO found that parents who brought in their children for TB diagnosis did so with the prompting and referral of Kiddie TB Patrollers.

Conclusion: Schoolchildren equipped with correct information on TB can become effective TB control advocates.

PD-1043-29 Engaging parliamentarians in TB control efforts: lessons from India

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Background and challenges to implementation: **Background:** Sensitizing and engaging political representatives is important in achieving policy level action on TB. They are key decision makers, critical to policy formation; act as advocates and also as independent reviewers of government TB control efforts. With more than 800 MPs, engaging parliamentarians on TB requires long term strategic approach and collective action. The Challenge TB project aims to galvanize action to establish a National TB Caucus with parliamentarians.

Intervention or response: Challenge TB launched the Call to Action for a TB Free India to mobilize a wide range of stakeholders to demand and sustain high level domestic commitment and resources to end TB in India. We organized an advocacy and sensitization consultation with parliamentarians through an existing parliamentary forum on population and devel-

opment issues. This was the first time this parliamentary group was sensitized on TB.

Results and lessons learnt: 20 members of the parliamentarians (MPs) pledged their support and commitment to work on TB with support from Indian Association of Parliamentarians on Population and Development (IAPPD). Parliamentarians will

1. Raise TB questions in Parliament
2. Advocate with party leaders & policy makers for increased resources on TB
3. Utilize MP fund & Saansad Adarsh Gram Yojana to
 - Provide financial support to TB patients and families;
 - Adopt slums/ villages and make them TB-Free;
 - Review TB control and care work in their constituencies

Conclusions and key recommendations: Collaborative action especially through engagement of existing parliamentary forums is a must for engaging people's representatives on TB and increase voice and action in the policy space. The Challenge TB team plans to bring all civil society organizations (including IAPPD GCAT & CLRA) engaging with political representatives together to form a India TB Caucus in the long term.

PD-1044-29 Community to clinic: community health workers successfully conduct home-based TB screening and facilitate linkage to care in rural South Africa

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Introduction: Tuberculosis (TB) is the leading cause of death among adults in South Africa, disproportionately affecting people with HIV. The World Health Organization estimates that one-third of TB cases remain undiagnosed. Novel strategies are needed to improve case detection and linkage to TB care, particularly in rural areas with chronic health system staff shortages.

Methods: Previously unemployed community members received training as lay community health workers (CHWs) and conducted home visits in their traditional Zulu communities in Umzinyathi District, KwaZulu-Natal, South Africa. They offered screening for TB, HIV, diabetes, and hypertension. Following a positive symptom screen for TB, CHWs collected a sputum sample for evaluation by GeneXpert and provided a referral letter for further TB investigation at a primary health care clinic. A

composite of patient self-report and laboratory data was used to determine linkage to care.

Results: From February 2015-December 2015, 2805 community members were visited at home by CHWs (mean 255/CHW), 1790 (63.8%) accepted screening for TB. Four hundred and six (22.7%) were identified with at least one of four TB symptoms (cough, weight loss, fever, night sweats). Of these, 317 (78.1%) were women, and median age was 50 (IQR 31.0-63.8). TB symptoms were not significantly more common in HIV-infected community members (53/196, 27.0%) compared to HIV-uninfected (353/1589, 22.2%, $P=0.13$); however, among those with HIV, TB symptoms were significantly more common in those not on ART (25/59, 42.4%) than those on ART (28/137, 20.4%, $P=0.003$). Among those with symptoms, CHWs collected sputum from 141 (34.7%) and referred 171 (42.1%) to a clinic for evaluation. One hundred and sixteen specimens (82.3%) were of sufficient quality for GeneXpert testing. Among those referred, 57 community members (33.3%) reported linkage to care and evaluation by a clinic nurse.

Conclusions: CHWs successfully identified community members with TB symptoms and facilitated sputum collection and linkage to care among hard to reach rural impoverished groups, including people with HIV who were not on ART. In highly TB- and HIV-prevalent, resource-limited regions, unemployed community members can be trained to function as CHWs and can be effective in expanding TB screening in their own communities.

44. Extra-pulmonary TB

PD-1045-29 Epidemiology of extra-pulmonary tuberculosis in Afghanistan

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Background: Afghanistan ranks among the 22 high burden tuberculosis (TB) countries in the world and around 13,000 Afghans die each year. DOTS as a strategy was introduced to the National Tuberculosis control Program (NTP) in 2002, followed by Stop TB Strategy and finally The End TB Strategy. Extrapulmonary Tuberculosis (EPTB) accounts for 22.7% of all TB cases in Afghanistan an area of low HIV prevalence. This is a cross-sectional retrospective review of the epidemiology of extra pulmonary tuberculosis in Afghanistan from 2009 through 2015. **Method:** As a cross-sectional retrospective study, we assessed the trend of EPTB in the country and the

geographic pattern and characteristics of the disease. We used data from National Tuberculosis Program (NTP) and included all cases of TB diagnosed in the Afghanistan between 2009, and 2015. Information on age, sex, year of diagnosis, anatomic location of the site of disease, was retrieved from the register.

Results: Totally 212,523 all form TB cases identified during 2009 - 2015, among them 164,151 (77.3%) had pulmonary TB and 48,215 (22.7%) of EPTB cases. Three provinces of Afghanistan, Kabul, Kandahar and Ghazni registered higher number of EPTB during the 7 years period (Kabul with 38%, Kandahar with 38% and Ghazni with 31% of EPTB). TB lymphadenitis and TB pleural effusion were the two most common types of EPTB and accounted for 67% of all EPTB, followed by genitourinary TB, Pott's disease, bone and joint TB and kidney TB. The average treatment success rate of bacteriologically confirmed TB cases from 2009 - 2014 was 89%, while the treatment completion rate of extra pulmonary patients was 91% in the same period. Extrapulmonary tuberculosis (EPTB) accounts for 25% of TB cases in areas of low HIV prevalence.

Conclusion: Afghanistan has a high proportion of patients registered as having EPTB, for whom treatment outcomes are satisfactory. Further work is needed to better understand how EPTB is diagnosed throughout the country. The satisfactory outcome of PTB and EPTB in Afghanistan is the proper implementation of Direct Observation Treatment (DOT) at health facility and community level.

PD-1046-29 Epidemiological assessment and profiling of EPTB cases registered under the national TB program in Himachal Pradesh state, India

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Background: Extra-Pulmonary Tuberculosis (EPTB) contributes a substantial proportion of TB case load registered under Revised National Tuberculosis Control Programme (RNTCP); on an average, one in five of registered tuberculosis patients has extra-pulmonary tuberculosis. However, due to its non-communicability unlike pulmonary TB, it has taken a back seat in disease control efforts. Diagnosis of EPTB is always been a challenge. Due to lack of clinical suspicion and diagnostic algorithm, under diagnosis and over diagnosis of EPTB is oftenly reported. With an overall objective to carry out the profiling of EPTB cases registered under RNTCP and to have their epidemiological assessment, the present study was carried out.

Methods: A cross sectional study was carried out in selected TB units in four districts of Himachal Pradesh in India. All registered 474 EPTB cases under

the program w.e.f. 01/01/2013 to 31/12/2013 across selected TB units were interviewed using a pretested semi-structured questionnaire by the investigators and all clinical records were also examined.

Results: Pleural effusion (41.9%) and lymph node (31.2%) were most common types of EPTB followed by abdominal (6.1%), meningeal (5.2%), pericardial (3.9%) and spinal (3.5%). There were average 3.1 (SD: 1.9; median: 3; IQR: 2.0-4.5) number of medical consultations before establishing a diagnosis for EPTB. Sputum smears examination and X-ray examination was carried out in 31.3% and 22.3% of patients respectively for EPTB diagnosis. Total 37 (7.8%) and 16 (3.3%) patients were investigated using with Computerized Tomography scan and Magnetic Resonance Imaging. FNAC was done in 158 (33.3%) patients; total 122 patients (77.2%) were declared positive as per the reports of FNAC. ADA was positive among 22 (13.9%) patients. Culture examination and molecular methods were not used in any of the EPTB cases put on treatment.

Conclusions: Overall, diagnosis of EPTB has been made as per the existing guidelines under the program, however markedly long delay has been reported in most cases before the final diagnosis and initiation of treatment. Newer molecular diagnosis tools such as CBNAAT should be judiciously deployed. Standards for TB care in India should be followed in diagnosis and treatment of EPTB cases.

PD-1047-29 The role of macrophages P2X7 1513 A-C and IL-10R1 S138G polymorphisms in susceptibility to extra-pulmonary tuberculosis in Indonesia

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Background: Indonesia is a country with high burden of tuberculosis with prevalence of 647 per 100 000 population. It is debatable whether tuberculosis is an inheritable disorder, a contagious disease, or a disease caused by poor living condition. According to its site of infection, tuberculosis is divided into pulmonary and extrapulmonary. Tuberculosis is caused by chronic interaction between immune system and intracellular organism. A single nucleotide polymorphism in the macrophage's P2X7 and IL-10 receptor genes have been reported to cause progression to extrapulmonary tuberculosis in several asian and african countries exclusively but they have not been studied in Indonesia.

Methods: This study is the final outcome of two polymorphism studies. DNA was isolated from subject's blood. Multiplex Polymerase Chain Reaction analysis of P2X7 1513 A->C and IL-10R1 S138G polymorphism were performed to subjects in

case control study. Case group: 24 subjects with Extrapulmonary tuberculosis (6 subjects have both extrapulmonary and pulmonary tuberculosis). Control group: 23 subjects with Pulmonary tuberculosis only.

Results: P2X7 1513A->C: Respectively, 5 (20.8%) and 12 (52.2%) AA genotype were observed in Case and Control group and 19 (79.2%) and 11 (47.8%) polymorphic AC genotype in Case and Control group. No polymorphic CC genotype was observed in both groups. The 1513C allele was strongly associated with extrapulmonary tuberculosis (OR=4.1; 95%CI =1.2-14.9). While in 12 healthy subjects with positive tuberculin test, we found 10 (83.3%) AA, 2 (16.7%) AC, and no CC genotype. IL10R1 S138G: Respectively, 21 (87.5%) and 19 (82.6%) AA genotype were observed in Case and Control group and 3 (12.5%) and 3 (13.0%) polymorphic AG genotype in Case and Control group. While 0 (0%) and 1 (4.3%) polymorphic GG genotype found in Case and Control. The IL10R1 G allele was not associated with extrapulmonary tuberculosis (OR=0.68; 95%CI =0.1-3.4). While in 12 healthy subjects with positive tuberculin test, we found 10 (83.3%) AA, 2 (16.7%) AG, and no GG genotype. Only 3 subjects have both polymorphism. The evidence of both polymorphism in a subject was not associated with increased susceptibility to extrapulmonary tuberculosis (OR=2.0; 95%CI =0.2-23.7) **Conclusions:** P2X7 1513 A->C gene polymorphism and the 1513C allele increases susceptibility to extrapulmonary tuberculosis. While IL10R1 S138G polymorphism is not associated with increased susceptibility.

PD-1048-29 Tuberculous lymphadenitis in Ethiopia predominantly caused by strains belonging to the Delhi/CAS Lineage and newly identified Ethiopian clades

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Background: Recently, newly defined clades of *Mycobacterium tuberculosis* complex (MTBC) strains, namely Ethiopia 1-3 and Ethiopia H37Rv-like strains, and other clades associated with pulmonary TB (PTB) were identified in Ethiopia. In this study, we investigated whether these new strain types exhibit an increased ability to cause TB lymphadenitis (TBLN) and raised the question, if particular MTBC strains derived from TBLN patients in northern Ethiopia are genetically adapted to their local hosts and/or to the TBLN.

Methods: Genotyping of 196 MTBC strains isolated from TBLN patients was performed by spoligotyping and 24-loci mycobacterial interspersed repetitive unit-variable number of tandem repeats (MIRU-VNTR) typing. A statistical analysis was carried out

to see possible associations between patient characteristics and phylogenetic MTBC strain classification. **Results:** Among 196 isolates, the majority of strains belonged to the Delhi/CAS (38.8%) lineage, followed by Ethiopia 1 (9.7%), Ethiopia 3 (8.7%), Ethiopia H37RV-like (8.2%), Ethiopia 2 and Haarlem (7.7% each), URAL (3.6%), Uganda I and LAM (2% each), S-type (1.5%), X-type (1%), and 0.5% isolates of TUR, EAI, and Beijing genotype, respectively. Overall, 15 strains (7.7%) could not be allocated to a previously described phylogenetic lineage. The distribution of MTBC lineages is similar to that found in studies of PTB samples. The cluster rate (35%) in this study is significantly lower ($P = 0.035$) compared to 45% in the study of PTB in northwestern Ethiopia.

Conclusion: In the studied area, lymph node samples are dominated by Delhi/CAS genotype strains and strains of largely not yet defined clades based on MIRU-VNTR 24-loci nomenclature. We found no indication that strains of particular genotypes are specifically associated with TBLN. However, a detailed analysis of specific genetic variants of the locally contained Ethiopian clades by whole genome sequencing may reveal new insights into the host-pathogen co-evolution and specific features that are related to the local host immune system.

PD-1049-29 Detection of mycobacteraemia in individuals with presume extra-pulmonary tuberculosis

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Background: Mycobacteremia was described as a future prospective of tuberculosis research and is a key event in dissemination. We did blood culture survey to measure the prevalence of *M. tuberculosis* bacteremia in extra-pulmonary tuberculosis cases.

Methods: Subjects with clinical suspicion of extra-pulmonary TB were recruited from various wards and outpatient departments of the institute during June 2008 to June 2011 for the diagnosis of tuberculosis. From the included individuals, 5 ml of intravenous blood sample was withdrawn and was directly inoculated in the BacT/ALERT® MB (bioMérieux, France) blood culture bottles and incubated in the MB/BacT system (bioMérieux, France). Flashed positive BacT/ALERT® MB culture bottles were removed and the cultures were subjected to blood lysis and subsequently sub-cultured for species identification and drug susceptibility assays.

Results: During the study period, a total of 338 subjects suspected of having extrapulmonary tuberculosis were screened and recruited, out of which 306 were included and the remaining were excluded

according to the exclusion criteria. Among the 306 cases, there were 153 (50%) males and 153 (50%) females with an overall mean age of 30.5 ± 14.3 years. All the 306 extrapulmonary samples were subjected for bacteriology investigation, of which 87 (28.43%) were bacteriological confirmed. Overall, MB/BacT blood culture positivity was detected in 36 (11.76%) patients. *M. tuberculosis* was isolated predominantly from blood in 34 (94.4%) and *M. avium* in 2 (5.5%) patients with mycobacteremia. The average days for isolating *M. tuberculosis* and *M. avium* in blood cultures were 20.54 ± 3.4 days and 12.2 ± 2.6 days respectively. Among bacteriology positive cases, mycobacteremia was detected in 23 (26.3%) whereas among bacteriology negative cases it was 5.93% ($n=13$). In HIV positive patients, mycobacteremia was detected in 11 (31.42%) while in HIV negatives patients 25 (9.22%) had mycobacteremia. Multidrug resistant isolates were detected in 20.5% of *M. tuberculosis* isolated from blood.

Conclusions: *M. tuberculosis* can cause bacteremia in a significant number of patients with extrapulmonary tuberculosis. Hence mycobacterial blood culture appears to be useful additional diagnostic tool in the early diagnosis of TB, particularly in the HIV infected and also in HIV-negative patients.

PD-1050-29 Assessment of lymph node tuberculosis in Tunisia: a national prospective study

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Background: The aim of this study was to estimate the incidence and possible risk factors of lymph node tuberculosis (LNTB) cases among presumed TB cases in Tunisia and to describe their microbiological profile.

Methods: A national cross-sectional prospective study on LNTB presumed TB cases was conducted by the National Tuberculosis Program -Ministry of Health-Tunisia (NTP) from February 2013 to December 2013. Demographic, risk factors, clinical, histological and laboratory data were collected using a pretested semi-structured questionnaire. Cases of LNTB were defined by the presence of positive culture and/or AFB smear for *M. tuberculosis* complex and/or histological findings.

Results: A total of 177 presumed LNTB cases were included in the study, among them, 159 (89.8%) were clinically diagnosed LNTB cases with an incidence of

8.21 cases per 100 000 inhabitants. Cases involved were living in 19 governorates in the North and the South of Tunisia. LNTB represented 52.7% of extra-pulmonary TB cases and 29.9% of TB cases all forms. The mean age was 31.3 ± 1.8 years and the sex-ratio was 0.4. The majority of patients (91.5%) were vaccinated with BCG. 17.2% had a past medical history of TB. Only 0.5% were receiving immuno-suppressive therapy. The concept of contact with animals was reported by one-third (32.2%) patients. Raw milk or unpasteurized milk consumption was registered in 71.9%. Anatomopathology showed good sensitivity in the diagnosis of LNTB (97.1%). Direct smear microscopy examination had poor sensitivity (11.3%). Cultures yielded positive results in 49.7% showing *M. bovis* in 78.7% of cases and *M. tuberculosis* in 19.9% of cases. All strains were fully susceptible to isoniazid, ethambutol and streptomycin, only 0.8% of *M. bovis* were resistant to Rifampicin.

Conclusions: The high rates of *M. bovis* compared to *M. tuberculosis* may explain the growing trend of the incidence of LNTB cases in Tunisia. Consumption of unpasteurized milk and dairy products could explain the predominance of this species. It is essential to strengthen the prevention strategy against bovine tuberculosis in livestock to interrupt its transmission to humans in our country.

PD-1051-29 Comparison of characteristics of extra-pulmonary and pulmonary tuberculosis cases in Kenya, 2011-2015: retrospective study

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Background: Tuberculosis (TB) continues to be a major global health problem. The clinical manifestations of TB varies with the most common involved organ being the lungs, although all organs can be affected. HIV epidemic has been held responsible for this proportional increase of extra-pulmonary TB. This retrospective study was designed to characterize and define the demographics and clinical presentations of pulmonary (PTB) and extra-pulmonary (EPTB) tuberculosis in Kenya between 2011 and 2015.

Methods: Patients who were treated for tuberculosis were evaluated retrospectively from secondary electronic data abstracted between January 2011 and December 2015. The patients were divided into two groups PTB and EPTB and demographic and clinical characteristics compared using tests for proportions

and Student's t-test. A *P* value of 0.05 was accepted as statistically significant.

Results: Of 366,771 registered cases, 64,090 (17.4%) were EPTB of whom 59239 (92%) were new cases. The female to male ratio was 2:1 for EPTB patients and 1:2 for PTB patients which was significant (*P* < 0.05). The mean age for EPTB and TB was 33 and 34 respectively. Proportion of EPTB subtypes was: Pleural effusion 18495 (30%), Adenitis 13008 (21%), military 6101 (9%), meningitis 1850 (3%), abdominal 2105 (3%) and other types 2154 (3%). Among the EPTB cases 16619 (26%) were not classified while pericarditis and urogenital accounted for the majority of cases of those classified. 11% (106) of females had urogenital TB compared to the 6% of the men. The HIV positivity rate was 34% for PTB and 38% for EPTB, with an ART (antiretroviral therapy) uptake of 90% and 89% respectively. The treatment success rate was 86% and 84% for PTB and EPTB respectively.

Conclusions: There were more females diagnosed with EPTB compared to males. Among the other types of EPTB, urogenital and TB pericarditis were among the most common. There is need for policy to strengthen Intensified Case Finding (ICF) and diagnosis for gynaecological TB among women and patients with pericarditis. A prospective study to determine the clinical presentation of pericarditis especially in the era of HIV needs to be conducted in Kenya.

PD-1052-29 Testicular tuberculosis: the experience of a tertiary centre in a high-incidence urban setting in the UK

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Background: Testicular tuberculosis (TB) is a rare presentation. In 2014, genitourinary TB accounted for 2 percent of cases in the UK. We report on a presentation of TB that is rarely referred directly to TB services.

Methods: A retrospective case review of Testicular TB from the national registry between 2007 and 2014 at two sites of a large urban tertiary referral centre in the UK.

Results: 19 cases were identified (mean age 42 years). 17 patients were referred from local urology services, one case was referred by his GP after investigation abroad and in one case the referral route was unknown. At presentation, 47% of patients (9/19) had testicular swelling only, 26% (5/19) had pain and swelling, of the remaining cases, one had increased

frequency of micturition and the other haematuria. In total, 9 of 19 had recently been treated for epididymo-orchitis. Only 21% (4/19) had systemic symptoms. All patients were investigated with an Ultrasound (US) Testes, 4 also had CT imaging. 14 of the 19 patients (74%) underwent a surgical procedure: 6 Orchiectomies, 5 biopsies, 2 incision and drainages, an epididymectomy and an exploration. 4 of 6 patients who had orchiectomies prior to referral to TB services presented with swelling only. The mean duration between presentation to secondary care and diagnosis was 12 months (IQR 3-15). In 68 percent of patients, the testicle was the only site of disease. The other patients had disseminated (pulmonary, adrenal and brain), Pulmonary (2), mediastinal lymphadenopathy (1) and renal (1) TB. Histology showed evidence of TB in all cases where reports were available. In 58 percent of cases samples were sent for TB culture, however where surgery was the first procedure only 3 of 10 patients had TB culture sent. 81 percent of TB cultures were positive (9/11) coming from Early Morning Urine (EMU) (4), surgical specimens (2), pus swabs (2) and sputum (1). All cultured organisms were fully sensitive.

Conclusions: The presentation of Testicular tuberculosis often mimics carcinoma. In high incidence settings, urine and surgical specimens should be considered for TB culture in the investigation of testicular symptoms.

45. 'Do you want to know a secret?' The rising incidence of non-tuberculous mycobacteria

PD-1053-29 Clinical significance of non-tuberculous mycobacteria isolated in a mycobacteriology laboratory in Delhi, India

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Background: Studies to assess the clinical significance and disease spectrum of Nontuberculous Mycobacteria (NTM) are far and few. The role of NTM as aetiological agents in the causation of pulmonary and extrapulmonary infections has seldom been systematically studied in India. Because of the large number of potentially pathogenic NTM that can be encountered in the clinical laboratory, a species identification of these organisms is required to ensure appropriate treatment. However, the labour intensive conventional methods of speciation are not used in every

laboratory, and hence NTM infections are often ignored.

Methods: We applied PCR-restriction fragment length polymorphism (PRA) technique for differentiation of NTM and *M. tuberculosis* complex. *Hsp65* and *Sau96I* PRA or Genotype Mycobacterium CM/AS were applied on the DNA extracted from cultures of acid fast bacilli ($n=1078$) isolated from patients suspected of suffering from pulmonary tuberculosis ($n=1075$), breast abscess ($n=1$) and skin and soft tissue infection ($n=2$).

Results: We could identify NTM in 300 (27.82%) isolates. Of these, 101 NTM could be potential pathogens based on clinical details of the patients. *M. intracellulare* were isolated from 27.72% (28/101), *M. fortuitum*/*M. smegmatis* in 15.84% (16/101), *M. fortuitum*/*M. senegalense* in 16.83% (17/101), while *M. kansasii* constituted 4.95% (5/101) of the isolates. *M. abscessus* was isolated from 15 (14.85%) isolates and *M. mucogenicum* constituted 1.98% (2/101) of the NTM. Finally, of the 101 NTM isolated, clinical significance was established in 32 (31.68%) isolates. Fifteen of the *M. intracellulare* isolates were obtained from repeated samples and were probably pathogenic. Nine isolates of *M. abscessus* were received from the sputum of four patients repeatedly. Two isolates of *M. abscessus* were obtained from pus samples. *M. mucogenicum* and *M. simiae* were isolated from the same patient in repeated samples, probably a co-infection of species. *M. fortuitum* was isolated from a single patient with an abdominal wall sinus.

Conclusions: Our results highlight the importance of speciation of Mycobacteria, not only for appropriate diagnosis, but also to rule out laboratory contamination. In conclusion, though the most common etiology of NTM disease is infections by *M. intracellulare*; the incidence of infections by *M. abscessus* is rising in Delhi.

PD-1054-29 Nationwide laboratory survey of uncommon mycobacteria isolated in Japan

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Background: The patients of non-tuberculosis mycobacteria (NTM) have been increasing in Japan, and the incidence (per 100 000) is reported as 14.7 in 2014 (Namkoong H. AJRCCM 191;2015:A5268). The NTMs are over 170 species, and the DNA-DNA hybridisation kit (DDH, Kyokuto Pharmaceuticals) identifies 18 mycobacterial species including *M. tuberculosis*, but many other uncommon NTMs are left unidentified. It will be useful to have the profile of NTM species isolated in our setting for the develop-

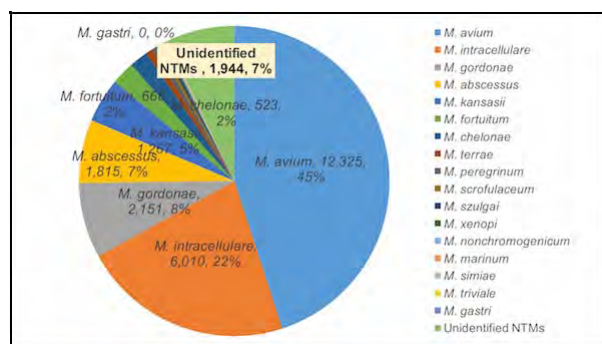
ment of new identification systems and the clinical management of the patients.

Methods: A total of 32,841 mycobacteria including 27,392 NTMs were isolated from dominant four laboratories over Japan in 2014, and approximately 7.1% of NTMs (1,944 isolates) were found unidentified. Then, we collect approximately 200 unidentified isolates in 2015 in order, and identify those species by 16S rRNA, *rpoB*, *hsp65* and so on.

Results: The major NTMs isolated were *Mycobacterium avium* complex (67%), *M. gordonae* (7.9%) and *M. abscessus* (6.6%) (Figure). A total of 30 NTMs were identified to date. They were 12 *M. lentiflavum*, 2 *M. cosmeticum*, 2 *M. mucogenicum*, 2 *M. phocaicum*, 2 *M. shimoidei*, 2 *M. shinjukuense*, and one each of other six species (*M. engbaekii*, *M. gordonae*, *M. intracellulare*, *M. mageritense*, *M. porcinum*, *M. seoulense*, *M. septicum*, *M. triplex*). As far as we searched, *M. cosmeticum* and *M. engbaekii* have not been reported in Japan.

Conclusions: The most frequent mycobacterial species identified from uncommon NTMs was *M. lentiflavum*, and species of rapid growers. We will report the general profile of uncommon NTMs in Japan.

Figure Breakdown of total 27 392 NTMs in Japan, 2014



PD-1055-29 Pulmonary non-tuberculous mycobacterial infection: 372 cases

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Background: Nontuberculous mycobacteria (NTM) are widespread in the nature/environment isolated from water and soil. With advanced microbiological methods, diagnostic capabilities, therefore, prevalence of NTM infections increased. Here we investigated patient records with NTM-positive sputum to identify clinical significance of NTMs.

Methods: NTM was detected in 372 patients at our hospital between 2009 and 2014 via rapid test on Löwenstein-Jensen medium and *P*-nitro- α -acetylaminob- β -hydroxypropiophenone test in Mycobacteria Growth Indicator Tube. Hsp65PCRREA was used for strain typing. Treatments, radiologic and bacteriological follow-ups, and comorbidities were evaluated. Patients' condition and treatment results were obtained via telephone calls and/or from the assigned tuberculosis dispensary.

Results: Among 372 patients (257 (69.1%) males; mean age of 54 ± 17 years), NTM strains was identified in 96 (25.8%). *Mycobacterium avium* complex was detected in 25 (26.04%), *M. abscessus* in 21 (21.8%) and *M. kansasii* in 15 (15.6%). Fifty-three (14.14%) NTM patients were diagnosed and treated according to American Thoracic Society guidelines; 76 (20.4%) received conventional therapy with major tuberculosis drugs; and 243 (65.3%) were followed-up without therapy, 196 (72%) of which had single mycobacterial growth in the culture. Among 53 treated patients, 32 (60.4%) had cured, 4 (7.5%) were continuing and 1 (1.9%) had discontinued treatment, 7 (13.2%) had died; 39 (73.6%) had tuberculosis history; 18 (33.9%) and 12 (22.6%) had pulmonary and non-pulmonary comorbidities. Nodular lesion, consolidation, and cavity were present in 9 (23.1%), 26 (49.1%), and 19 (48.7%), respectively, of the 39 patients receiving NTM therapy who had radiological evaluation.

Conclusions: Identifying NTM strains ensures correct treatment approaches. Standard treatment approaches are needed for NTM diagnosis and treatment, clinical significance and incidence of which is rising.

PD-1056-29 Prevalence of non-tuberculous mycobacteria among presumptive TB cases in Namibia

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Background: Non-tuberculous mycobacteria (NTM) are frequently present in cultured sputum specimens from presumptive TB cases. In many Sub-Saharan African countries such as Namibia, the prevalence has not been quantified. The local laboratory networks often refer to positive isolates from MGIT which are negative for mycobacterium TB as NTMs, but does not perform routine identification of the species. As a consequence, the prevalence of the different NTM species is also unknown. The objective of this assessment was to determine this

prevalence among patients submitting sputum for TB diagnosis.

Methods: Sputum specimens collected from presumptive TB cases in Namibia over a period of 10 months were subjected to mycobacterial culture with MGIT if positive on smear microscopy or Xpert MTB/Rif. Culture isolates that had a positive growth but a negative mycobacterium tuberculosis identification using the BD MGIT TBc[®] Identification Test and yet positive on smear microscopy were regarded as having NTMs. These NTM isolates were then forwarded for identification using GenoType Mycobacterium CM/AS[®] test (HAIN)

Results: A total of 253 isolates from 4171 presumptive TB cases were identified as having NTM. This represented a prevalence of 6% of cultured specimens. The prevalence was higher among those previously treated (89/955, 9%) than among new patients (159/3153, 5%) with an Odds Ratio of 1.9 (1.5-2.5). There was also a marginally higher prevalence of NTM among those HIV infected vs those that were not (OR 1.3; 1.0-1.8). 155 of these were successfully confirmed as follows; *M. intracellulare* -104 (67%), Unidentified mycobacterial species- 27 (17%), *M. scrofulaceum*-8 (5%), *M. avium*- 5 (4%), Mixed species: 5 (3%) and other- 6 (4%). The odds of having *M. intracellulare* were significantly higher in those with previous treatment for TB at 2.7 (1.4-5.7). The clinical significance of these results was not immediately determined.

Conclusions: Growth of NTMs may occur in almost 10% of mycobacterial cultures from previously treated presumptive TB cases in SubSaharan Africa, and the clinical relevance of this must be explored. Majority of NTMs in Namibia are *M. intracellulare*, which happens to be more common among patients previously treated for TB.

PD-1057-29 Identification and drug susceptibility profiling of non-tuberculous mycobacteria species from sputum smear-positive pulmonary cases in Ghana

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Background: Nontuberculous mycobacteria species are emerging important pathogens. This study aimed to identify NTMs isolated from smear positive sputum samples from Ghana and analyse the susceptibility to streptomycin (STR), isoniazid (INH) and rifampicin (RIF).

Methods: A prospective study was conducted between August 2012 and July 2014. One thousand seven hundred and fifty-five mycobacterial isolates

were obtained from 2149 pulmonary TB cases. Specie identification of NTMs was done using hsp65 gene sequence after DNA sequencing of the amplified gene and similarity search by Blasting. Patient variables were then compared among the species identified.

Results: Forty-three isolates (2.5%) were identified as NTMs: 5 (11.6%) *M. abscesses*, 13 (30.2%) *M. avium*, 3 (7.0%) *M. colombiense*, 18 (41.9%) *M. intracellulare*, 3 (7.0%) *M. phocaicum* and 1 (2.3%) *M. Sherrissii*. Sixteen of the isolates were from female patients (37.2%) and the remaining 27 (62.8%) were males. The average age of all the patients was 39.4 years (min=10, max 75 years). From 25 patients (10 females and 15 males) with indicated HIV status, 13 (52.0%) were positive. Females infected with NTMs were more likely to be HIV positive (7/10) compared to males (6/15) males (OR=3.3). HIV positivity was highly associated with NTMs (52.0%) as compared to MTBC (5.8%) ($P=0.0000$, OR=6.6, 95%CI=2.7-16.2). 46.2% of the known HIV positive patients harboured *M. avium* followed by 38.5% *M. intracellulare*. Twenty-five patients indicated presence or absence of BCG scar out of which 16 (64.0%) had scar and 9 (36.0%) had no scar. All the 43 NTMs were resistant to INH, 16 were resistant to the 3 drugs, 20 resistant to INH and RIF, 3 resistant to STR and INH. Only 7 were susceptible to RIF whereas 24 were susceptible to STR. The 5 *M. abscesses* were resistant to all 3 drugs whereas all the *M. avium* strains were resistant to INH and RIF but only 3 were resistant to STR. Among the *M. intracellulare* strains, resistance to STR, INH and RIF were 8, 18 and 15 respectively.

Conclusions: Considering the prevalence and the observed high resistance, it is important to consider NTMs in the global efforts to control TB.

PD-1058-29 Diagnosing NTM in immunocompetent chronic lymphadenitis cases: an emerging entity

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Background: Cervical lymph node infection associated with nontuberculous mycobacteria (NTM) in immunocompetent patients is an emerging problem globally. Traditionally diagnosis is done through clinical examination, pathological finding or ZN microscopy of lymph node aspirated samples, which altogether indicate mycobacterial infection only, unable to differentiate *Mycobacterium tuberculosis* from NTM infection. Increasing incidence of lymph node tuberculosis cases prompted us to look for NTM in these samples. This study aimed to diagnose nontuberculous mycobacteria from patients of chron-

ic cervical lymphadenitis and its clinical and pathological association.

Methods: Total 154 cases were recruited having chronic cervical lymph node swelling between January - December, 2014. Therein detailed history and thorough clinical examination of patients were reviewed. The aspirated samples were subjected for Ziehl Neelsen (ZN) smear stain examination, May Grunwald - Giemsa stain and MGIT culture. Positive cultures were primarily identified by cord formation in ZN smear examination, detection of MPT-64 antigen by immuno-chromatographic test (S D Bioline). Non tuberculosis mycobacteria were identified by using different biochemical reaction and morphological features.

Results: Out of total suspects 7/154 (4.5%) were identified as non-tuberculous mycobacterial lymphadenitis. Clinical examination showed that all the seven cases were presented with lymph node swelling, fever and previous ATT history. Other features seen were pain (2/7; 28%), pus discharge (3/7; 42%) and montoux positive (3/7; 42%). The most common species identified was *M. chelonae* (3/7, 42%) followed by *M. fortuitum* (2/7, 28%), *M. abscessus* (1/7, 14%) and *M. terricomplex* (1/7, 14%). Four patients were managed surgically, one with surgical resection and medical treatment while 2 patients went missing.

Conclusions: Non tuberculous mycobacteria should be looked for in non responding patients with cervical lymph node. Rapid growers are important etiological agents in cervical lymph node swelling. Proper diagnosis and appropriate treatment help in better management and early recovery of patients.

PD-1059-29 Molecular diagnosis of non-tuberculous mycobacteria at the Centre d'Infectiologie Charles Mérieux, Mali

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Background: Nontuberculous mycobacteria (NTM) typically reside in soil and water. But can cause a wide array of clinical diseases to humans particularly in immunocompromised patients. Of the more than 150 NTM species reported in the literature, about 30 have been strongly associated with diseases. The diagnosis of NTM is complex and requires good laboratory facilities and good communication between biologists and clinicians. The role of the NTM in diseases is scanty in resource limited settings.

Methods: This study was conducted from January 2009 to December 2014 at the Laboratoire Rodolphe Mérieux of Centre d'Infectiologie Charles Mérieux-

Mali (CICM). We collected biological samples from patients seen at different clinics and hospitals in Bamako and received at CICM for tuberculosis diagnosis. Samples were from pulmonary (sputum) and extra pulmonary (urine, aspired fluids, pus) origin. Aspired fluids consisted of cerebrospinal fluid, pleural fluid, joint fluid and peritoneal fluid. Contributing samples were collected and registered with SYSLAM 64 software (CODAT informatique, France). Samples were first decontaminated and concentrated by high speed centrifugation, then stain with Ziehl-Neelsen for microscopy. Solid media (Löwenstein-Jensen) and liquid media (Bact/ALERT3D) were inoculated. Molecular identification and susceptibility to rifampicin and isoniazid were performed using the Genotype MTBDRplus and GenoType Mycobacterium CM/AS kits (HAIN Lifescience, Nehren, Germany) on positive cultures. Data were computed and analyzed by SPSS v19.0.1.

Results: A total of 1467 samples were tested with 44.6% sputum and 31.9% of aspired fluids. 162 samples were positives for mycobacteria by culture (117 sputum, 22 aspired fluids, 14 pus, 6 urines, 3 gastric aspirations). 18 NTM were isolated with 5 *M. fortuitum* (3 sputum, 1 urine, 1 pus), 4 *M. abscessus* (3 sputum, 1 urine), 1 *M. intracellulare* (sputum), 1 *M. mucogenicum* (sputum), 1 *M. smegmatis* (sputum) and 6 *M. spp.* (5 sputum, 1 aspired fluid) which need further testing for identification.

Conclusions: NTM may play an important role in human diseases and should be considered as cause of morbidity and mortality in resource limited settings. Since isolation of the organism does not necessarily indicate clinical infection, communication between biologists and clinicians is important to coordinate the diagnosis.

PD-1060-29 Spectrum and susceptibility pattern of non-tuberculous mycobacterial infections in Pakistan: 2012-2015

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Background: With the roll-out of anti-tuberculous drugs and Xpert® MTB/RIF across Pakistan, there is an increase in non-tuberculous mycobacterial (NTM) disease, as seen by rising isolation rates at the Aga Khan University Clinical Laboratories, Karachi, Pakistan. We describe here the risk factors and characteristics of patients with NTM disease, their spectrum and susceptibility pattern.

Methods: From Jan 2012 to April 2015, 245 samples yielded NTM on routine bacterial and mycobacterial cultures: 228 were pulmonary and 17 extrapulmonary. Information on underlying lung disease, history

of tuberculosis, surgery and other trauma were compiled from retrieved clinical records maintained as per laboratory practices. The spectrum of pulmonary and extrapulmonary NTMs were described and their susceptibility rates to clarithromycin, moxifloxacin, linezolid, imipenem and amikacin were determined. Identification of the NTM was based on growth rate, pigment production and selected biochemical tests and susceptibilities were performed by broth microdilution method as recommended by CLSI (M24-A2, 2012).

Results: Of the 228 pulmonary isolates, 84 were nonchromogenic slow growers (74 confirmed *M. avium-intracellulare* complex), 38 photochromogens (35 confirmed as *M. kansasii*), 2 scotochromogens, 65 Rapidly Growing Mycobacteria (12 confirmed as *M. abscessus* and 9 as *M. fortuitum*) and 39 NTM, not further identified. Of these patients, male:female ratio was 1.7, 80% were adults, 16% elderly and 3.5% children. Underlying lung disease was present in 21% of those whose status was known ($n=81$). Amongst those who had been evaluated for tuberculosis ($n=111$), 67% had prior history of TB and some form of anti-tuberculous therapy. There were 17 cases of extra-pulmonary NTM isolates: 13 were RGMs and 4 slow growers (3 *M. kansasii*). Majority of these were isolated from skin and soft tissue and other post-surgical infections ($n=13$). For all NTMs tested, susceptibility to amikacin was 100%, clarithromycin 88%, linezolid 89%, moxifloxacin 52% and imipenem 19%.

Conclusions: The spectrum of pulmonary and extra-pulmonary NTM disease is different: *M. avium* dominating in pulmonary disease especially in post-TB patients, while nosocomially acquired RGMs in extrapulmonary infections. The mainstay of therapy in both types of NTM disease is clarithromycin and amikacin, with linezolid a better third agent than moxifloxacin or imipenem.

PD-1061-29 Distribution of pulmonary NTM cases in the Information System for Special Tuberculosis Treatment (SITE-TB), Brazil, 2010-2015

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Background: Non-tuberculosis mycobacteria (NTM) have a large distribution in the environment and can be the cause of infections in humans, very similar to tuberculosis, but with a difficult diagnosis and distinctive treatments.

Methods: The data were extracted from Information System of Tuberculosis Specials Treatment (SITE-TB) in March, 2016, all cases of NTM between 2010-2015. All cases that presented in the molecular

identification only *M. tuberculosis* complex were excluded.

Results: Between 2010-2015, Brazil notified on SITE-TB 1,298 NTM cases. 352 (27.1%) showed negative sputum and positive culture, 177 (13.6%) showed positive sputum and culture, 618 (47.6%) were identified by molecular biology test and 1,085 (83.6%) showed pulmonary form. 258 (19.9%) cases occurred in HIV positive patients, 18 (1.4%) cases in patient with silicosis and 198 (15.3%) cases were tobacco users. The more prevalent species were *M. kansasii* with 238 (18.3%) cases, followed by *M. avium* 192 (14.8%) and *M. abscessus* 126 (9.7%), even with 110 (8.5%) cases were identified as *M. avium* complex and 60 (4.6%) cases as *M. abscessus* complex. Furthermore, species like *M. intracellulare*, *M. fortuitum* and *M. chimaera* were detected with 6.9%, 3.6% and 3.5% respectively. In 88 (6.8%) NTM cases were not possible to do the identification test and 209 (16.1%) showed other species of NTM. As shown by literature, the *M. avium* and *M. avium* complex were more prevalent in HIV patients, having appeared in almost 27% and 16% of patients, respectively.

Conclusions: There is a diversity of species involved in the infection by NTM. The classification as *M. abscessus* complex should be more investigated because the treatment is a challenge in the pulmonary form. Like seen in other countries/studies, *M. kansasii* was the most prevalent species and the coinfection with HIV is very prevalent. Several species were identified only the complex level, but the molecular identification is very important to determine the specie, the appropriate treatment and to understand the epidemiological distribution of them.

46. Optimising drugs for resistant TB

PD-1062-29 Safety and efficacy of tioureidoiminomethylpyridinium perchlorate in treatment of pulmonary MDR-TB

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Background: In accordance with international classification Tioureidoiminomethylpyridinium perchlorate (TTP) belongs to thioacetazone group [D.Tomas, 2014]. TTP in vitro demonstrated significant inhibiting effect on viability of drug-resistant mycobacteria strains of TB. Wherein MIC of the substance varied from 0.78 to 6.25 µg/ml. TTP presented high protective and therapeutic effect in dose 30 mg/kg equivalent to Isoniazid and Amikacin,

stronger than Ethambutol and Ciprofloxacin; and in dose 20 mg/kg - similar to Ofloxacin.

Objective: To confirm efficacy and safety data on tioureidoiminomethylpyridinium perchlorate (TTP) in treatment of multidrug resistant (MDR) lung tuberculosis in adults.

Methods: 147 adult patients at the age of 18-65 years with MDR lung tuberculosis with bacterial excretion were treated at St.Petersburg Research Institute of Phthisiopulmonology in 2013-2015. Ist group included patients treated with TTP on the top of standard anti-TB therapy ($n=100$), IInd group ($n=47$) - patients treated by standard therapy only. TTP was used in the Ist group during 6 months of intensive phase, and further on standard therapy only with overall treatment duration 18 months. Safety data was collected by assessment of clinical signs and laboratory analysis; efficacy data - by cessation of bacterial excretion. Statistical analysis was performed using SPSS 16.0.

Results: Adverse drug reactions (ADRs) were registered in 38,0% (38) in the Ist group - on therapy with TTP, and in 29,8% (14) in the IInd group - on standard therapy. In the Ist group the most common ADRs were endocrine disorders (18.4% (9) vs (0), $P < 0,01$) and fever (8.2% (4) vs (0), $P < 0,05$) - which were not observed in IInd group. Other ADRs were recorded in equal measures in both groups. Efficacy of treatment (which was assessed by cessation of bacterial excretion in sputum) was higher in Ist group vs IInd group: after 3 months of treatment (68.0 % (17) vs 37.5% (9), after 6 months - (80.0% (20) vs 62.5% (15), and after 18 months - (88.0% (22) vs 66.7% (16).

Conclusions: Efficacy of treatment with TTP was 88.0% in complex with other anti-tuberculosis drugs while its addition on the top of standard therapy does not relevantly influence its safety.

PD-1063-29 Adverse events in linezolid treatment of pulmonary TB caused by extensively drug-resistant *Mycobacterium tuberculosis*

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Background: Within recent years there has been increasing of number of patients with TB caused by extensively drug resistant MBT (XDR-TB). Efficiency of XDR-TB treatment is complicated.

Objective: To determine adverse events while treatment of XDR-TB with linezolid.

Methods: in St-Petersburg research institute of phthisiopulmonology in 2013-2015 49 patients with XDR lung TB, from 18 to 60, male and female were examined. Linezolid was used in 24 patients with

extensive drug resistance 600 mg per day intravenously, by drop infusion (Ist group) with combination of 5-6 anti TB drugs taking into account range of MBT drug resistance in intensive phase. Control group ($n=25$), used 5-6 anti TB drugs without linezolid. Statistical analysis was performed with application of a χ^2 .

Results: By 6 months of therapy symptoms of tuberculosis intoxication were not detected among all patients both in basic and control groups. Adverse drug reaction were noted with equal frequency in both groups (29.1% (7) against 32.0% (8). In patients who used linezolid, hepatotoxic reactions occurred in 4 of 7 patients; 3 patients developed haematotoxic reactions: leukopenia, neutropenia and Hb decrease. In control group - hepatotoxic reactions (5 of 8), dyspepsia (3 of 8). When symptomatic therapy was applied adverse drug reaction were resolved. Therapy continued until 8 months as an intensive phase. Cessation of of bacterial excretion was registered in the group with linezolid significantly more often than in control group: (62.5% (14) against 36.0% (9), ($P > 0.05$).

Conclusions: The number of adverse events when linezolid use is not higher than for standard therapy. When including linezolid in scheme of XDR-TB therapy cessation of bacterial excretion by 6 months is twice more often than therapy without its inclusion.

PD-1064-29 When is the right time to add new and repurposed medication for treatment of pre-XDR and XDR-TB?

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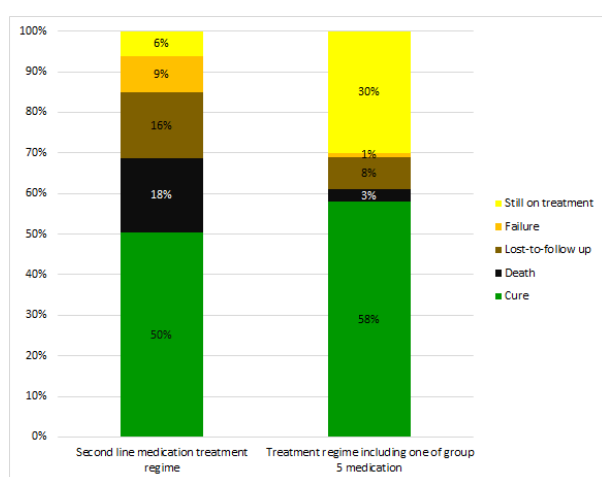
Background: MDR-TB we can treat successfully with 2nd line drugs with good cure rates. But when *M. tuberculosis* has resistance to injectable (INJ) and/or fluorquinolon (FQ) it is more difficult to achieve favourable treatment outcome. Group 5 medications - Linezolid (Lzd) in Latvia was introduced in 2008, Bedaquiline (Bdq)-2013 and Delamanid (Dlm)-2014. **Methods:** Data were collected: sputum culture conversion time (Cc), HIV status, DST, treatment duration and outcomes. Patients were divided in two groups. Group one patients received one of group 5 medications: Lzd alone, Bdq or Dlm with or without Lzd and group two-who used other 2nd line drugs. Statistical analyses were made using SPSS.

Results: From 2011 till 2015 50% of all diagnosed MDR-TB cases had pre-XDR and XDR-TB. 81% (200) were male and 19 % (48) were female with median age 41 and 39 years. Overall treatment results are: 53% cured, 13% died, 13% lost-to- follow up, 7% failure and 13% are still on treatment. 77 patients (31%) has received one of group 5 medications-Lzd

alone 30% ($n=23$), Bdq 52% ($n=40$) and Dlm 18% ($n=11$). Resistance pattern in both groups were similar. Majority of patients (79%) achieved stable Cc-median time 60days. Comparing both groups-cure rates are significantly ($P < 0.001$) higher 58% versus 50% in patients who received new medications. 88% of patients who are still on treatment have achieved stable Cc. In 2nd group was higher death rate and lost-to-follow up-respectively 18% v. 3% and 16% v. 8%. Analysing patients who died-median treatment time for them was 76 days and significantly more of them (79%) were HIV positive with disseminated TB. Median time when Tx was adjusted was 68 days.

Conclusion: Adding new group 5 medications: Lzd, Bdq or Dlm in Tx cure rate is significantly higher and almost all patients who are still on treatment has achieved stable Cc with also possibly favourable outcome. HIV positive person with disseminated TB has less chance to be cured.

Figure Treatment outcomes in both groups



PD-1065-29 Determination of plasma levels of levofloxacin by high performance liquid chromatography for use at a multidrug-resistant tuberculosis hospital in Tanzania

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Background: Therapeutic drug monitoring may improve multidrug-resistant tuberculosis (MDR-TB) treatment outcomes. Levofloxacin demonstrates significant individual pharmacokinetic variability. Thus, we sought to develop and validate a high-performance liquid chromatography (HPLC) method with

ultraviolet (UV) detection for levofloxacin in patients on MDR-TB treatment.

Methods: The HPLC-UV method is based on a solid phase extraction and a direct injection into the HPLC system. Plasma was loaded onto Oasis SPE cartridges, conditioned, washed and eluted. Eluents were then evaporated and the residue reconstituted in 100 μ L of 5% acetonitrile for HPLC separation. The assay parameters of accuracy, precision, recovery and limits of quantification were determined using human plasma spiked with known concentrations of levofloxacin. This method was then utilized to measure levofloxacin concentrations from patients' plasma samples from a retrospective cohort of consecutive enrolled subjects treated for MDR-TB at the national TB hospital in Tanzania during 5/3/2013- 8/31/2015.

Results: The use of phenacetin as an internal standard improved accuracy (relative standard deviation, RSD, 13%). The recovery was $92 \pm 7\%$. The limits of quantification were 0.25 μ g/mL for levofloxacin. Among MDR-TB patients, plasma was collected at 2 hours after levofloxacin administration, the time of estimated peak concentration (eC_{max}). Forty-one patients had plasma available and 39 had traceable programmatic outcomes. Favorable outcomes were achieved in 26/39 (66.6%) patients although only 13/41 (31.7%) patients reached the expected literature derived C_{max} of greater than 8 μ g/mL. There was a non-significant trend of a more rapid mean time to sputum culture conversion in weeks (5.17 [3.46] vs. 6.80 [3.61], $P=0.20$) as well as a greater likelihood of cure (53.8% [7/13] vs. 34.6% [9/26], $P=0.25$) in those patients with $eC_{max} > 8$ μ g/mL. Furthermore, one patient with a eC_{max} /minimum inhibitory concentration (MIC) of 1.13 μ g/ml at 4 weeks acquired extensively drug resistant (XDR)-TB while undergoing treatment.

Conclusions: The HPLC-UV methodology for determination of levofloxacin concentrations achieved excellent accuracy and reproducibility along a clinically meaningful range. The individual variability of levofloxacin concentrations in MDR-TB patients from Tanzania supports further study of the application of onsite therapeutic drug monitoring and MIC testing.

PD-1066-29 Additive effects of cotrimoxazole in the treatment of XDR-TB in a mouse model of experimental tuberculosis

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Setting: The complexity of XDR-TB treatment and its low efficiency is largely due to the limited arsenal of effective anti-TB drugs. Development of new anti-TB

drugs is a time-consuming and extremely expensive. Another way is reinforcing TB treatment regimens by the use of the additive antibacterial agents. However, empirical antibiotic treatment is not always successful, so we used microbial control agent efficiency.

Methods: The study is based on experimental studies on 60 albino mice, female, average weight 28-30g. Animals were infected with the MTB (0.1 ml of a bacterial suspension containing 10^8 /ml cells). It was selected high virulent clinical strain from genetic family Beijing with an XDR but susceptible to cotrimoxazole (MIC 1.9/65 mcg/ml). The range of sensitivity to anti-TB drugs was determined by the minimum inhibitory concentrations. Additive to isoniazide (H) drug is co-trimoxazole (SXT). Drugs were administered daily for 4 weeks after 2 weeks TB infection. Regimens (-mg/kg): H-25; SXT-250; H-25/Sxt-250; H-25/Sxt-500; H-0/SXT-0-control, which corresponds to H-5, SXT-1980, SXT-2*1980 human doses and provides an effective co-trimoxazole for selected strain. The effectiveness of the regimen was assessed by lung MTB contamination relative to the control after 1 month of treatment.

Results: During the experiment, there has been the death of three mice at 5-6 weeks after infection in the control group due to the progression of TB. There were no significant differences between all groups of mice weight change. Modes of H-25 and Sxt-250 reduced lung contamination by 22% and 65% respectively, H-25/Sxt-250 Mode - by 78%, H-25 / Sxt-500 mode - by 87%.

Conclusions: This is preliminary data for reinforced regimens TB treatment development based on the microbiological and pharmacokinetic parameters. Co-trimoxazole may potentiate the regimen for XDR-TB treatment. In drawing up such a regime it needs the microbiological monitoring of the effectiveness of the drug influence on the strain.

PD-1067-29 The prolongation of bedaquiline-containing regimens for MDR/XDR-TB: effectiveness and safety

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Background: The regimens for MDR/XDR-TB treatment designed for 18 months at least, whereas bedaquiline (Bdq) administration is limited to 6 months. However, Bdq is essential for adequate treatment regimen (min 4 TB drugs), limited by drug resistance and/or intolerance. The effectiveness of Bdq is evident, but the safety is not yet clear, especially in advanced cases and extensive comorbidity.

Methods: The prospective unblinded non-randomized study included 70 pts, finished 24 weeks of Bdq-

treatment; in 43 of them Bdq was prolonged until 36 weeks and then in 24 - until 48 weeks. These 70 pts were 18-75 y. o., 67.2% male, 21.4% new and 78.6% re-treated cases. Lung cavities detected in 85.7%, bilateral damage - in 62.9%, XDR - in 55.7%, pre-XDR - in 34.2%. Concomitant diseases diagnosed in 91.4%, alcohol abuse - in 24.3%, intravenous drug-use - in 15.7%. Bdq combined with 4-6 TB-drugs, most common (75.7%) linezolid, cycloserine/terizidone, fluoroquinolones. The adverse events (AE) definite by Division of Microbiology and Infectious Diseases (DMID) criteria.

Results: The 24-weeks Bdq-treatment was successful in 58 pts (82.9%), defaulted in 4 (5.7%), in 4 (5.7%) Bdq excluded due to seriously AE (SAE - III-IV DMID) and in 6 (8.6%) with large cavities (>3.0 cm) and bilateral involvement the culture conversion wasn't obtained. The time until conversion (IQR 2.0-11.5) prolonged in similar patients too. At the end of 36th week of Bdq the culture conversion obtained additionally in one and at the end of the 48th week - in two pts more (the total success rate up to 87.1%). In total, at 24th week, 149 episodes of AE obtained in 60 pts (85.7%), include SAE in 14 pts (20.0%). At the end of 36th week additional 20 episodes of AE and 5 pts with SAE were obtained and at the end of the 48th week - 14 episodes and two pts with SAE more.

Conclusions: The 24-weeks Bdq-containing regimens is high effective by culture conversion, whereas cavities and lung tissue infiltration maintained in most patients. The continuation of the treatment with Bdq can provide in these patients the additional treatment success and is reasonably safe.

PD-1068-29 Third anti-tuberculosis drug in the continuation phase for TB patients: is it the need of the hour for India?

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Background: India has the world's largest burden of tuberculosis (TB) and India's national program has recorded an optimal treatment outcomes in >85% of the target populations. India's national program is planning to implement a TB regimen that will include 3 anti-TB drugs-isoniazid, rifampin and ethambutol-in the continuation phase to prevent development of multidrug resistant (MDR)-TB among patients with isoniazid mono-resistance. We aimed to assess whether such a strategy is supported by the baseline TB strain drug resistance patterns in western India.

Methods: We prospectively enrolled adults suspected to have primary pulmonary TB (defined as new TB

diagnosis without a prior history of TB) in BJ Government Medical College, Pune, India between December 2013 and December 2015. All pulmonary TB suspects underwent two sputum smears, cultures and Xpert® MTB/RIF assays. If the baseline cultures were positive, drug susceptibility testing (DST) was performed using the proportion method including testing for isoniazid, rifampin, ethambutol and streptomycin. We assessed the relative frequency of mono- and multiple-TB drug resistance.

Results: Of 766 TB suspects assessed, 417 had positive cultures at baseline and 383 DST results were available. Of these, 249 (65%) were males and median (IQR) age was 31 (interquartile range, 24, 43) years. Isoniazid, rifampin, ethambutol and streptomycin mono-resistance was found in 11 (3%), 6 (2%), 1 (0.1%) and 16 (4%) patients, respectively. Any isoniazid resistance (without rifampin resistance) was seen in 25 (7%) patients, of which 14 (56%) had additional streptomycin and/or ethambutol resistance. MDR-TB (defined as resistance to at least isoniazid and rifampin) was found in 16 (4%) patients. Resistance to all 4 drugs tested was seen in 10 (3%) patients.

Conclusions: Our cohort identified a relatively low isoniazid mono-resistance. Therefore whether or not there is a clear benefit of using three drugs in the continuation phase remains unknown and should be further studied.

PD-1069-29 A model of bedaquiline's exposure-response relationship and predicted effects of drug-drug interactions

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Background: The efficacy of bedaquiline in treatment of MDR-TB has been demonstrated with time to sputum culture conversion (TSCC) and month 30 cure-rates, but no relationship between bedaquiline exposure and efficacy has been identified. We aimed to characterize this relationship by modeling serial measures of mycobacterial load and utilize a model to evaluate potential impact of drug-drug interactions.

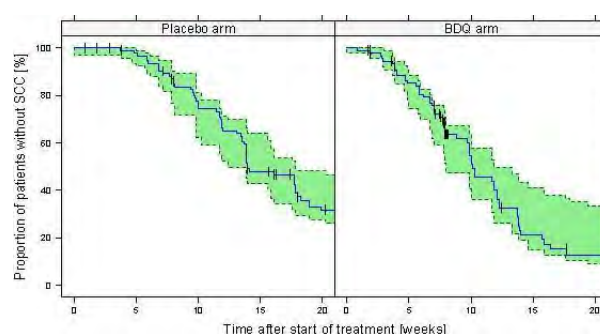
Methods: Quantitative mycobacterial load data (time to positivity [TTP] in MGIT) were obtained from a published Phase IIb study investigating the addition of either placebo or bedaquiline to an optimized background regimen in treatment of drug-resistant TB. A dataset including 6330 observations (59.8% positive) from 193 individuals collected unto week 20 was used for model building. Non-linear mixed effects models were developed in NONMEM7.3. Individual exposures were obtained from a separate pharmacokinetic model. The clinical importance of

covariates, quantified by changes in TSCC and proportion without SCC at week 20, was assessed through simulations. Furthermore, the impact of coadministration of ritonavir-boosted lopinavir, efavirenz and rifampicin was investigated.

Results: The final model included three simultaneously fitted components: a longitudinal representation of mycobacterial load in patients, a model of probability of bacterial presence in a sample, and a time-to-event model of TTP. The joint model described data well and a posterior predictive check demonstrated that TSCC was well predicted. Early bedaquiline exposure ($AUC_{0-24h, day14}$) was found to significantly affect the half-life of mycobacterial load. Median TSCC is predicted to be 5 weeks shorter for high vs. low exposures. Additionally, baseline TTP was found to be a significant covariate and patients with (pre-)extensively drug-resistant TB to clear mycobacteria slower. Bedaquiline $AUC_{0-24h, day14}$ is typically expected to increase 18-31% during coadministration with lopinavir/r, decrease 20-28% with efavirenz and decrease 48-59% with rifampicin. For typical subjects, the predicted corresponding relative changes in proportion of patients without SCC at week 20 are about -15%, +17% and +45%, respectively.

Conclusion: The presented model provides the first characterization of bedaquiline's exposure-response relationship and shows that higher bedaquiline levels lead to faster bacterial response. The model can inform development of novel anti-TB regimens and application in patients, including those coinfectd with HIV.

Figure Posterior predictive check of TSCC



PD-1070-29 Analysis of the treatment effect of regimens containing different fluoroquinolones in MDR-TB patients

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Background: To compare and analyze the treatment effect and outcome of the regimens containing different fluoroquinolones in the MDR-TB patients so as to provide the basis for the rational choice of fluoroquinolones in the treatment of MDR-TB.

Methods: The 232 MDR-TB patients were diagnosed and included in this study respectively in ten hospitals of China between July 2009 to July 2010. Among them, 124 patients were treated with the regimen containing Moxifloxacin (Mfx group) and 108 patients were treated with the regimen containing Levofloxacin (Lfx group). We collected the bacteriological and radiological data in different period of treatment. The effect and outcome of treatment were evaluate at the end of treatment.

Results: 1) In the MDR-TB patients who could be got qualified sputum samples to be tested, the rate of sputum culture conversion were similar between two groups in the end of intensive phase ($P>0.05$) and the rate of sputum culture conversion of the Lfx group was higher than it of the Mfx group in the end of continuation phase ($P<0.05$). 2) In the end of continuation phase, the rate of cavity closure in the Lfx group was higher than it in the Mfx group and the improvement rate of pulmonary lesion were similar between two groups ($P>0.05$). 3) The rate of adverse reaction during the treatment was similar between two groups, of which the rate of liver injury were highest. 4) The successful rate was similar between two groups, 60% and 61% respectively. The mortality rate of the Lfx group was less than it of the Mfx group (0.9% vs 6%) and the loss rate of the Lfx group was higher than it of the Mfx group (24% vs 15%). 5) Logistic analysis showed that the factors associated with the treatment outcomes were the lesions >3 lung fields, treatment >2 times and course of disease ≥ 2 years ($P<0.05$).

Conclusions: The effect and outcome of Moxifloxacin and Levofloxacin were similar in the treatment MDR-TB. The lesions range, treatment times and course of disease associated with the treatment outcomes in the MDR-TB patients.

47. MDR- and isoniazid-resistant TB: outcomes

PD-1071-29 Treatment outcomes for multidrug-resistant tuberculosis patients under DOTS-Plus in developing counties: systematic review and meta-analysis YM Mesfin¹ ¹Haramaya University, Public Health, Harar, Ethiopia. e-mail: mogesyoni@gmail.com

Background: Anti-tuberculosis drug resistance is a major public health problem that threatens progress made in tuberculosis care and control worldwide. The successful treatment rate for multi drug resistant tuberculosis patients is a key problem that cannot be ignored. The findings and conclusions of previous studies on directly observed treatment, short course (DOTs) including effectiveness are inconsistent and not well addressed. Therefore, it is very important to assess and summarize the overall treatment outcomes for multi drug resistant tuberculosis under DOTS-Plus program in recent years. The purpose of this study was to assess and summarize the available evidence for multi drug resistant tuberculosis treatment outcomes under DOTS-Plus in developing countries.

Methods: Systematic review and meta-analysis of the published literature of studies was conducted. Original studies were identified using databases of Medline/Pubmed, EMBASE, and Google Scholar. Heterogeneity across studies was checked using Cochran Q test statistic and I^2 test. The pooled estimates of treatment outcomes were computed using random effect model.

Results: Based on the 14 observational studies included in the meta-analysis, 5600 patients reported treatment outcomes, 63.5 % (58.4%, 68.5) of patients met the definition of success full treatment (cured or treatment completed) with a pooled cure rate of 55.6 %, whereas 12.6% (9.0,16.2) of patient had died, 14.2% (11.6,16.8) defaulted from therapy and 7.6% (5.6,9.7) failed therapy. The overall percentage with unsuccessful outcomes was 35.4 % (30, 40.8). Unsatisfactory high unsuccessful treatment outcomes, 43 % (32, 54) was observed among patients who were in the standardized treatment regimens.

Conclusions: This meta-analysis revealed that patients exhibited very low multidrug resistant tuberculosis (MDR-TB) treatment success rate compared to the WHO 2015 target. The high default rate identified could possibly be a potential source for the spread of MDR-TB strain in the population. On the other hand better treatment success rate was observed among patients in individualized treatment regimens than standardized ones. To improve the treatment outcomes of patients with MDR-TB, continuous supervision, monitoring, and counseling during follow up and default tracing at the household level is imperative.

PD-1072-29 High treatment success in patients started on multidrug-resistant tuberculosis treatment in Kenya

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Background: In March 2006, the first multidrug-resistant tuberculosis (MDR-TB) treatment program was implemented in Kenya. We describe patients' outcomes and adverse events.

Methods: Retrospective review of program data. Patients started on MDR-TB treatment from May 2006 to May 2012 were included. Treatment initiation occurred in 3 sites: Mathare clinic in an urban slum of Nairobi, Homa Bay District Hospital in a rural area of Western Kenya, and Kenyatta National Hospital (KNH) in Nairobi. Treatment regimens included 4 drugs (Kanamycin, Levofloxacin, Prothionamide, Cycloserine) during the intensive phase in KNH and 5 drugs (additional *P*-aminosalicylic acid) in Mathare and Homa Bay for a minimum of 6 months. The continuation phase comprised the same drugs without the injectable antibiotic for a minimum of 15 months. In Mathare and Homa Bay regimens were individualized according to the second line DST.

Results: Of the 169 patients included, 55.0% were men, median age was 29 years, HIV positivity was 25.4% and median BMI was 16.9. Baseline culture was positive in 92.6% (151/163) patients. Median time to culture conversion was 2 [IQR:2-3] months. Adverse events occurred in 67.4% of patients. Median time to onset was 1 month [IQR:0-4]. The most common were: 45.9% of patients with nausea/vomiting, 43.9% with electrolyte disturbance, 41.8% with gastritis and 31.6% with hypothyroidism. There was no difference in the number of adverse events and the time to the onset by gender, age group, BMI and HIV status. Treatment outcomes in 145 patients with final outcome known were: 76.6% success, 14.5% death, 8.3% lost to follow-up, and 0.7% treatment failure. The median time to death and default was 4.1 [IQR:2.0-15.9] and 11.0 [IQR:4.1-12.9] months respectively. Treatment success was 83.9%, 76.2% and 69.4% in Mathare, Homa Bay and KNH respectively ($P=0.162$). Individuals HIV-positive (OR:3.4, 95%CI 1.1-10.7) and men (OR: 2.8, 95%CI 1.0-7.6) were more likely to have an unfavourable outcome while those with culture conversion were less likely (OR:0.08, 95%CI 0.03-0.26).

Conclusions: Treatment success was high in this HIV prevalent population. Almost half the patients

presented with electrolyte disturbance and one third with hypothyroidism, which is unusually high and supports systematic close biological monitoring in Kenya.

PD-1073-29 Treatment outcomes among multidrug-resistant tuberculosis cases at a referral hospital for infectious diseases in Italy

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Background: MDR-TB is emerging as a major challenge for tuberculosis control programs and is becoming extensively widespread today, even in high-income countries with low TB incidence. In Italy the proportion of MDR-TB reported during 2013 was 3.3%; unfortunately, treatment outcomes in MDR-TB patients are poorly documented.

Aim: To evaluate the outcomes of MDR-TB patients treated at the National Institute of Infectious Disease (INMI), a referral hospital for Infectious Diseases in Italy.

Methods: 74 MDR-TB patients diagnosed between 2008 and 2015 were consecutively enrolled in an observational retrospective cohort study. All patients were treated according WHO guidelines.

Results: The patients (median age 35.8 yr) were mainly male (63.5%) and foreign born (87.2%). Among 74 patients, 2 were extensively drug-resistant (XDR) cases, 2 patients were HIV-coinfected, and 45 (61.0%) were newly diagnosed. Fifty-eight (78.4%) cases were pulmonary sputum smear-positive. 51% of patients were transferred in from units of other regions of central and southern Italy. Among 57 patients who completed treatment in the study period, 68.4 % achieved treatment success, 22.8% were lost to follow up, 3% were transferred out and 1.8% died.

Conclusion: Monitoring the treatment outcome of MDR-TB is essential to evaluate the effectiveness of interventions and to identify potential barriers for TB control. In our cohort MDR-TB is mainly related to the immigration of patients from countries with a high TB prevalence with a high proportion of new cases. Data show that, in a referral center for the treatment of MDR-TB, success rates close to the target defined by WHO can be achieved. However

actions to implement strategies to reduce the high proportion of patients lost to follow-up are needed in order to improve treatment outcomes.

PD-1075-29 Outcome of new cases of drug-resistant tuberculosis in Brazil

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Background: The cases of tuberculosis with drug resistance difficult and prolong the treatment of the disease. The Special Treatment Information System for Tuberculosis (SITE-TB) in Brazil is the main tool of surveillance of tuberculosis cases that require special treatment in Brazil.

Methods: A descriptive cross-sectional study of cases of drug resistant tuberculosis (TBDR) in the year 2013 was conducted. Was used the SITE-TB database. The cases were classified according to the pattern of resistance: mono drug resistance, poly drug resistance, multidrug resistance and extensive drug resistance.

Results: Were diagnosed in the year 2013 a total of 731 new cases of TBDR. Of these, 158 (21.6%) were mono drug resistance, 59 (8.1%) were poly drug resistance, 502 (68.7%) were multidrug resistance, 6 (0.8%) were extensively drug resistance, and 6 (0.8%) the resistance pattern were not defined. There was a predominance of males (67.9%) in the 35-44 age group (24.6%). The percentage of cure among new cases of TBDR was 60.9%, and 63.1% among multidrug resistant, 62.7% among poly drug resistance, 53.8% among mono drug resistance and 16.7% among extensive resistance. A high percentage of cases lose the treatment follow up (19.3%), of which 22.2% mono drug resistance, 18.9% multidrug resistance and 18.6% poly drug resistance. It should be highlighted that there were 49 (6.7%) deaths in total TBDR cases. The higher percentage of deaths (50%) occurred in extensive resistance tuberculosis cases.

Conclusion: The occurrence of TBDR in the country among people in working-age and male is worrying, especially in cases of multidrug resistance. Cases of mono drug resistance had the worst percentage of cure and loss of follow up, an important factor that may be contributing to the increase in resistance pattern. The higher percentage of deaths in cases with extensive drug resistance points to the need to strengthen early diagnosis of the cases, with the expansion for culture exam and sensitivity testing for both first and second drugs line, in order to avoid new resistance drugs tuberculosis cases.

PD-1076-29 Factors associated with treatment outcomes in a Brazilian isoniazid-monoresistant tuberculosis cohort

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Background: Although multidrug-resistant (MDR) tuberculosis is a global threat, monoresistance, in particular to Isoniazid, is more frequent. In Brazil, Isoniazid-monoresistance is treated with 2RZES₅/4RE or 2RZES₅/4RES₂. We analyzed treatment outcomes of Isoniazid-monoresistant tuberculosis in the Brazilian special treatment information system (SITE-TB) according to regimens.

Methods: SITE-TB registers, since 2010, all treatments different from RHZE for any indication. In March 2016, we searched all Isoniazid-monoresistant cases in SITE-TB. Those still 'under treatment' having started before March 2015 ($n=4$) were considered lost to follow-up, those having started since then were excluded ($n=52$). Treatment outcomes were classified as successful (cure/treatment completed) or unsuccessful, defined as (i) failure/death/loss to follow-up, or (ii) failure/death. Failure included patients who developed poly-drug resistance or MDR or 'changed regimen' during treatment. Odds ratio (OR) for successful/unsuccessful outcomes were calculated, adjusted (aOR) in a backward stepwise multivariate model for sex, age group, ethnicity, schooling, type of resistance (acquired versus primary), presence of cavity, bilateral disease, smear status at diagnosis, HIV and diabetes. Regimen remained in the final model regardless of statistical significance.

Results: Out of 311 Isoniazid-monoresistant cases, 52 were excluded. Successful treatment rate was 64.1% and was more likely among those with primary resistance [aOR=3.3 (1.9-6.0)], HIV-negative [aOR=3.2 (1.1-10.1)] and smear-negative [aOR=2.8 (1.3-6.3)] patients and, surprisingly, those with diabetes [aOR for non-diabetics/diabetes=0.3 (0.1-0.9)]. When excluding losses to follow-up ($n=46$), successful outcomes were more likely among smear-negative patients [aOR=4.2 (1.2-14.8)] and those with primary resistance [aOR= 3.2 (1.4-7.2)]. The regimen was not associated with outcomes [aOR=1.5 (0.7-2.9); 1.7 (0.7-3.8) excluding losses to follow-up]. MDR and 'changed regimen' were the main reasons for more unsuccessful outcomes with 2RZES₅/4RES₂. **Conclusions:** Isoniazid-monoresistant tuberculosis in Brazil has low rates of successful treatment. More attention should be addressed to this problem, especially in HIV, acquired resistance, and smear-positive patients. Regimens containing Streptomycin in the maintenance phase do not increase the

likelihood for success, probably because decision is made at the end of the second month when follow-up is adverse. Because culture is not compulsory at diagnosis in Brazil, all resistant cases may have been missed, unknown cases may have successfully used the standard regimen.

PD-1077-29 Treatment success rate of Programmatic Management of Drug-Resistant Tuberculosis in Himachal Pradesh, India: a retrospective study

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Background: Programmatic management of drug resistant TB (PMDT) under the Revised National Tuberculosis Control Program (RNTCP) is being implemented in Himachal Pradesh state (pop; 7 million) in India since 2011 and two drug resistant tuberculosis treatment (DRTB) centres have been established in the state. This study examines the treatment success of MDR-TB patients put on second line anti-TB drugs/Cat IV regimen in two DRTB centres in Himachal Pradesh.

Methods: In April 2015, a retrospective analysis of routine reports under the program for treatment outcome of MDR-TB patients cohort who were registered and put on second line anti-TB drugs between 1st quarter 2011 and 3rd quarter 2012 at the DRTB centre Dharampur and DRTB Centre Tanda was done. Meantime delay for diagnosis and treatment was also calculated.

Results: Total 112 MDR-TB patients were registered during this period. Overall treatment success rate among the registered patient was 45% which includes cure rate of 7 % and treatment completion rate of 38%. Near one-fourth of patients died during the course of treatment. About 10% patients defaulted during the treatment. Near 5% of patients stopped the treatment due to adverse drug reactions (ADR). Two patients were switched to regimen for XDR-TB, whereas 14 (13%) patients were still on treatment. There was a delay in diagnosis and initiation of treatment in both centres.

Conclusions: The overall treatment success rate of 45% in Himachal Pradesh is less than the national average of 48%, and far behind from the global target of 75%; delayed diagnosis and delayed initiation of treatment is one of the reasons for high death rate but warrants a detailed death audit under the program. Rapid scale-up of rapid molecular diagnostic services for drug sensitive and drug resistant tuberculosis with facilities for drug sensitivity testing of second line is also needed for the state. The default rate can be further reduced by intensifying health education activities, improving family support and implement-

ing social support programs, also an intense monitoring, early identification and management of ADR is needed to reduce default rates.

PD-1078-29 Outcomes of retreatment cases of drug-resistant tuberculosis at the Indus Hospital, Karachi

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Background: Treatment of drug resistant cases of tuberculosis is difficult, expensive and prolonged. The situation is worse while treating those patients who were previously treated for drug resistant tuberculosis (DR TB) but failed.

Objectives: To find out the treatment outcomes of DR TB patients who were declared failure of treatment, and then re-enrolled for added or modified

Methods: All patients enrolled under the Programmatic Management of DRTB (PMDT) sites managed by The Indus Hospital Karachi from 2010-2016 were included in the study. Patients whose treatment outcome was not declared, or transferred out were excluded. National TB Program guidelines were strictly followed during the whole course of treatment.

Results: A total of 2331 patients were enrolled on DR TB treatment, 234 (10%) patients were previously treated for DR TB while 95 (41%) failed. After excluding those who were still under treatment or transferred out; 49 patients were included in the study, 28 (57%) were female; 43 (88%) patients were previously exposed to first line drugs and 30 (70%) were failed, the median age was 26 years (range 15-61) and the median number of drugs on the regimen was 8 (6-11). The mean treatment duration for those declared cured was 22 months (18-30) and for failed cases it was 6 months (6-30). 24 (49%) patients were resistant to fluoroquinolones. The resistance patterns of the study group were as follows: 39 (76%) multiple drug resistant; 10 (24%) extensive drug resistant. The re-treatment outcomes were as follows: 24 (49%) cured, 13 (27%) died, 8 (16%) failed and 4 (8%) lost to follow-up.

Conclusion: The overall success rate of re-treatment of previously failed DR-TB patients is 49%, which is unacceptable. Therefore, we suggest introduction of new, safe and effective anti-TB drugs and novel regimens for faster sputum conversion, less toxic and more effective treatment of patients who failed on conventional DR-TB regimens.

PD-1079-29 XDR-TB treatment outcomes in European regions of the Russian Federation

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Background: The Russian Federation has biggest number of detected and registered for treatment number of XDR-TB cases. 845 XDR-TB cases were registered for treatment in 56 regions of European part of Russia in 2012.

Methods: Cohort analysis of XDR-TB patients' treatment outcomes in 24-36 months after the start of treatment on second-line drug regimen

Results: Standard WHO recommended report on treatment outcomes for XDR-TB patients showed treatment success rate in 23.7%. Treatment failed 25.1%, died 23.6%, lost to follow-up 17.4%, not evaluated due to continuation of the treatment 10.5% of XDR-TB patients. Treatment outcomes for XDR-TB cases in different geographical clusters of European part of Russia (see Table). Proportion of XDR-TB cases who was still on treatment after 24-36 months fluctuated in different clusters from 24.5% in regions of Southern Russia to 4.5% in regions of Central Russia.

Conclusions: Treatment success rate for XDR-TB cases according WHO recommended report comprised 23.7% but 10.5% patient are still on treatment behind reporting period. It demands to use additional evaluation of XDR-TB cases treatment outcomes in 36-48 months after the start of the treatment (Current calendar year minus four).

Geographical clusters	Treatment success rate	Treatment failed	Died	Lost to follow-up/ Not evaluated
South of Russia and North Caucasus	24.0%	22.8%	18.2%	10.5%/24.5%
Nord West of Russia	19.7%	20.5%	28.7%	21.3%/9.8%
Central Russia	28.2%	25.6%	16.4%	19.2%/4.5%
Volga river cluster	19.3%	28.8%	26.4%	18.2%/7.3%

PD-1080-29 Description of attributes of multidrug resistant tuberculosis cases in Afghanistan: a cross-sectional explanatory assessment

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Background: Afghanistan contains 1,250 drug-resistances TB in a year. National TB program (NTP) started diagnosis and treatment of MDR-TB since

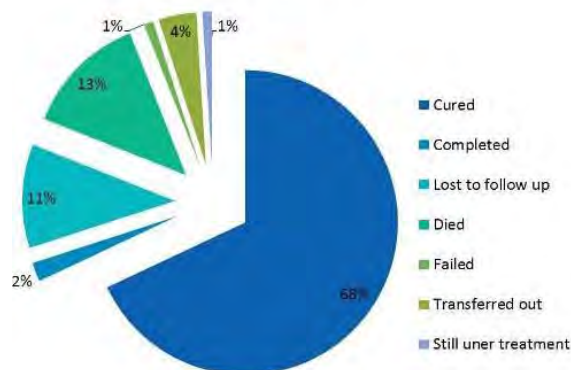
2011. However, features of MDR-TB were not understood. The aim of this assessment was to describe attributes of MDR-TB cases and their treatment outcomes.

Methodology: The assessment team reviewed the data from 2010-2015 and used MDR-TB registers and reporting forms, transferred data to SPSS and analyzed. The sample size was all MDR-TB cases registered and started treatment.

Results: During 2011-2015, NTP registered and started treatment to 297, 171 (58%) female and 126 (42%) male, MDR-TB cases. Mean age was 35.7 year and 100 (33%) among 15-24 years, 85 (28.6%) in age group 25-34, 47 (15%) in age 35-44, 9% (28) and 20% (36) among over 55 years. Also, 295 (99%) were pulmonary and 2 (1%) were extra pulmonary TB cases, of them, 224 (75%) had failed in category II and 11 (4%) had relapsed before diagnosed as MDR-TB. Further, time from onset of symptoms till diagnosis and treatment for 58 (20%) was less than one year, for 144 (48.4%) was between 1-2 year, for 85 (29%) was between 3-4 year and for 5 (1.6%) was more than five years. Moreover, 107 (36%), 42 (39%) male and 65 (61%) female, MDR-TB patients completed their treatment period and outcomes were 70% treatment success rate, 11% defaulted, 13% died, 1% failed, 4% transferred out and 1% still under treatment.

Conclusion: MDR-TB affected people at younger age and pulmonary compared to extra pulmonary TB cases were more likely to develop drug resistance. Also, there was delay from symptoms onset till diagnosis. Also, there was higher proportion of loss-to-follow up and transferred out rate. Thus, we recommend expansion of MDR-TB diagnosis and treatment to rests of country and testing of TB cases failed in first category.

Graph 1: Treatment outcomes distribution of MDR-TB patients in Afghanistan.



PD-1081-29 Outcome in MDR-TB patients treated under the Revised National Tuberculosis Control Programme of India

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Background: Programmatic management of drug resistant tuberculosis strategy (PMDT) under Revised National Tuberculosis Control Program of India (RNTCP) has become the cornerstone for management of MDR-TB in India. The strategy is operational nearly over last 4 years and is now covering whole country through a network of drug resistant TB centers (DRTB). The results of PMDT have now started coming in, but still not much data is available yet. Hence the present study was undertaken to evaluate the profile and outcome of MDR-TB patients treated under PMDT of RNTCP of government of India.

Methods: A total 105 confirmed MDR pulmonary tuberculosis patients were registered at our Chandigarh DRTB center through Jan 1, 2012 to Dec 31, 2013. They were treated with Category-IV, a standard 24 months daily directly observed MDR-TB regimen. These patients hailed from Chandigarh and Haryana state, the 2 provinces of north India. The patients were treated in the OPD after initial 7-10 days of hospitalization. A strict watch on treatment compliance and other progress parameters was kept through out.

Results: There were 62 males and 43 females. Their mean age and weight was 31 years and 42.8 kg respectively. Eighteen patients gave smoking history and 10 had diabetes. All had past history of anti-tubercular treatment and 75 had taken ≥ 2 such treatment courses. Out of 105 patients, 57 were declared cured and another 3 had successfully completed treatment. Thus, overall successful outcome was seen in 57.14% cases. Contrary to the belief, presence of diabetes or smoking was not associated with poor outcome, as well, serious adverse drug reactions to second line TB drugs was not a problem.

Table Treatment outcome of 105 MDR-TB patients

Treatment Outcome	n
1. Cure	57
2. Treatment completed	03
3. Default	06
4. Death	14
5. Shifted to XDR	10
6. Failure	05
7. Transferred out	10

Conclusions: The preliminary results show an overall satisfactory outcome in MDR-TB patients treated under PMDT strategy of RNTCP of India, however, a post treatment follow up will answer the relapse rate.

Presence of diabetes was not associated with poor outcome in MDR-TB.

48. MDR treatment outcomes

PD-1082-29 Impact of fluoroquinolone resistance on multidrug-resistant tuberculosis treatment outcomes: retrospective cohort study in Pakistan

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Background: Fluoroquinolones (FQs) are the most important second-line drugs for MDR-TB treatment. Therapeutic options for FQ-resistant (FQ-R) MDR-TB are very limited. The purpose of the present study was to determine treatment outcomes and risk factors associated with unfavourable outcomes of MDR-TB (excluding XDR-TB), focusing on the impacts of FQ-R status in the context of Pakistan.

Methodology: A retrospective cohort study was carried out including MDR-TB patients' (other than XDR-TB) enrolled at all programmatic management of drug resistance tuberculosis (PMDT) treatment sites of Pakistan between 2010 and 2013 with known treatment outcomes. Medical records were retrospectively reviewed for demography, TB treatment history, AFB cultures and drug susceptibility test (DST) results, treatment modalities and outcomes. 3166 MDR-TB patients, including 1364 (43%) FQ-R MDR-TB cases were included. Treatment outcomes were evaluated according to WHO 2013 recommendations. The DST to determine the sensitivity pattern was done on ofloxacin as per regular practice in the country.

Results: The treatment success rate in all MDR cases including FQ-R (3166) was 70%. The treatment success rates were poorer in patients with FQ-R (cure 61% and complete 1%) than in MDR-TB with FQ-S (cure 72% and complete 4%). Death rate is higher in FQ-R as compared to FQ-S patients (20% and 12% respectively). Similarly, treatment failure rate is higher in FQ-R (6%) as compared to FQ-S (3%).

Conclusion: FQ plays a very important role in curing the MDR-TB patient. FQ resistance results in poorer treatment outcome in patients with MDR-TB.

PD-1083-29 Modelling the effect of reduced regimen duration for multidrug-resistant TB in Karakalpakstan, Uzbekistan

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Background: Multidrug-resistant tuberculosis (MDR-TB) is a major threat to global tuberculosis (TB) control and poses particular problems in former Soviet states such as Uzbekistan, in Central Asia. Conventional treatment for MDR-TB typically has a high pill burden, lasts twenty months and often leads to unsatisfactory outcomes, while simplifying treatment is expected to improve success rates and reduce transmission. A shorter regimen, incorporating isoniazid, kanamycin, prothionamide, a late generation fluoroquinolone, ethambutol, pyrazinamide and clofazimine and lasting 9-11 months, has shown high success rates among selected MDR-TB patients in different settings, including Karakalpakstan, an autonomous region of Uzbekistan.

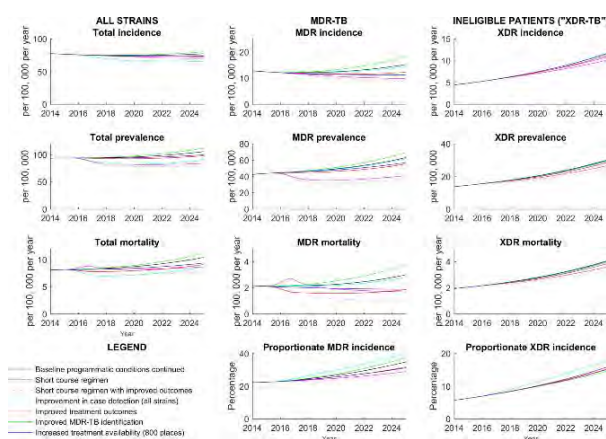
Methods: We present a mathematical model to estimate the likely impact of a short course regimen for MDR-TB in Karakalpakstan. The model builds upon an existing compartmental model of TB transmission to incorporate the additional features of strains with higher levels of drug resistance and correct or incorrect strain identification. We calibrate the model to local epidemiology and simulate reduction in the MDR-TB regimen duration from 24 to 10 months. Next, we compare the impact of this intervention on disease burden against the following four alternative programmatic responses: improvement in case detection for all strains, improvement in treatment outcomes for MDR-TB, improvement in strain identification for MDR-TB and increased treatment availability from 400 to 800 treatment places.

Results: Based on empirical outcomes among selected MDR-TB patients and unchanged treatment success rates, the short course regimen reduced MDR-TB incidence from 15.2 to 9.7 cases per 100 000 per year and MDR-TB mortality from 3.0 to 1.7 deaths per 100 000 per year in 2025, achieving gains comparable to or greater than the four comparator interven-

tions. Moreover, if treatment outcomes improved to reach those reported by van Deun et al. in 2010, further reductions in MDR-TB incidence and mortality to 8.7 and 1.0 per 100 000 per year respectively would be achieved.

Conclusions: Shorter regimens for MDR-TB bear the promise of individual benefits, including the potential for fewer adverse effects and a shorter intensive phase during which injections are required. However, such regimens also have the potential to improve public health outcomes and reduce transmission of resistant strains.

Figure Scenario outcomes



PD-1084-29 Treatment outcomes of pulmonary MDR-TB in the Tokyo metropolitan area, Japan

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Background: The prevalence of tuberculosis (TB) in Japan has been constantly decreasing since the 1960s, but still 19,615 TB cases were newly registered in 2014. A nationwide drug resistance survey conducted in 2007-2008 reported that the frequencies of multidrug-resistant (MDR) TB isolates from new and previously treated patients were 0.4% and 4.1%, respectively. However, treatment outcomes of recently diagnosed MDR-TB have not been assessed. The purposes of this study are to clarify the current epidemiological status of MDR-TB patients and to elucidate their treatment outcomes in the Tokyo metropolitan area, Japan.

Methods: Patients diagnosed with pulmonary MDR-TB and treated at hospitals in the metropolitan area Tokyo, Kanagawa, Saitama and Chiba prefectures of

Japan, between January 2011 and December 2013 were included in this study. Treatment modalities including linezolid and delamanid, treatment duration and treatment outcomes were evaluated. We used treatment outcomes as defined by the WHO.

Results: In the three-year period under study, a total of 54 TB cases were analyzed as MDR: median age was 42.0 years, 55.5% were male. Twenty five (46.3%) patients were new cases and 29 (53.7%) were previously treated cases. Among the MDR-TB, 2 (3.7%) cases showed resistance to LVFX and KM. Japanese patients were 27 (50.0%) and foreign-born patients were 27 (50.0%), most coming from high TB burden Asian countries. HIV was positive in one foreign-born patient. MDR-TB patients were treated with a median of five drugs for a mean of 640 days. Surgical resection was performed in 17 patients (31.5%). LVFX was prescribed for 43 patients (81.1%), linezolid for 9 (17.0%) and delamanid for 3 (5.6%). Treatment was successful in 41 MDR-TB patients (75.9%): 26 (48.1%) cured and 15 (27.8%) completed treatment. A total of 13 patients were classified as having unfavourable treatment outcomes. Five patients died during the course of treatment, 2 failed, 3 lost to follow-up, 3 returned to home country without culture negative conversion.

Conclusions: Among recently registered pulmonary MDR-TB in the Tokyo metropolitan area, three fourths of patients were successfully treated, but the return of foreign-born MDR-TB patients to their home countries before completion of treatment might be a problem.

PD-1085-29 Evaluation of the effectiveness and tolerability of two short-course treatments for multidrug-resistant tuberculosis in Niger

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Background: To evaluate the effectiveness and tolerance of two short course standardized regimens (12 and 9 months) for proven MDR-TB cases previously untreated with second-line drugs.

Methods: This retrospective study, conducted in Niger, included patients treated from 2008 to 2010 with a 12 to 14-month regimen and from 2011 to 2013 using a 9 to 11-month treatment. The regimens included clofazimine, ethambutol, pyrazinamide and high dose of gatifloxacin throughout, supplemented by kanamycin, prothionamide and medium-high doses of isoniazid during 4 to 6 months of the intensive phase. Patients were monitored by smear

and culture at start and monthly. Cured patients were followed-up every 6 months during 2 years.

Results: We included and analysed 65 patients under 12-month (mean duration 12.1 ± 0.2) and 55 under 9-month (mean 9.1 ± 0.2) regimens. One of the 58 patients following 12-month treatment tested for HIV (1.7%) was positive and 5 of the 55 tested patients (10%) under the 9-month arm had a positive test. Eighty-nine of the 120 subjects (74.2%) were severely affected ($BMI \leq 18.5 \text{ kg/m}^2$). Cure was obtained for 58 patients with 12-month regimen (89.2%; IC95%: 81.7-96.7) and for 48 (87.3%; IC95%: 78.5 - 96.1) with 9-month treatment. We found no failures in the 12-month arm and 2 in the 9-month one. Both patients had initial resistance to fluoroquinolones and pyrazinamide. No significant difference was found in term of outcome. In the 12-month arm, 41 of 65 patients (63.1%) had adverse events (AEs) versus 38 of 55 (69.1%) in the 9-month arm. Six patients (14.6%) in the 12-month arm required to stop or to reduce the dose of the offending drug versus 3 (7.9%) in the 9-month without significant difference between the two arms. All 49 patients assessed at 24 months follow-up after cure remained culture-negative with 12-month treatment with no relapses. Forty-two patients under 9-month arm remained culture negative and there were 2 relapses in patients with initial resistance to quinolones and pyrazinamide without significant difference in the two arms.

Conclusion: Standardized 12 and 9-month treatments for MDR-TB were equally effective in patients not previously exposed to second-line drugs. Adverse events were common but rarely severe.

PD-1086-29 Cause of death among MDR-TB patients enrolled in a national MDR-TB treatment program in Ethiopia

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Background: MDR-TB treatment in Africa is associated with the highest mortality of any region among patients who receive therapy globally. Though HIV co-infection and severe malnutrition have been identified as risk factors predictive of death in several cohorts, little is known regarding the cause of death among MDR-TB patients enrolled in a treatment program in the African context.

Methods: Retrospective chart review and descriptive case series of all deceased patients enrolled in a MDR-

TB treatment program in Ethiopia from February 2009 to December 2012 with at least 24 months of follow-up by December 2014. Cause of death was ascertained by clinicians caring for the enrolled patients.

Results: From February 2009 until December of 2012, 612 patients were initiated on second-line drugs and enrolled in MDR-TB treatment in two sites in Ethiopia and had ≥ 24 months of follow-up from a cohort with high cure and completion (79.9%). Among the 612, 85 died (13.9%), median age of 30 (IQR 25-40), median number of prior TB treatments was 2 (IQR 2-3), and 27 (32%) were HIV co-infected. Median BMI among 54 patients was 15.85 (IQR 13.55-16.7) who had a recorded BMI. Median time to death was 4.4 months (IQR 1.5-14 months). The causes of death were TB-related in 45 (48.2%) (respiratory failure, massive hemoptysis, pneumothorax, *cor pulmonale* or complications of CNS TB); HIV-related in 7 (8.2%); related to adverse drug effects in 15 (17.6%) (renal failure, electrolytes, neuropsychiatric effects and hepatotoxicity), or due to other causes in 22 (25.8%).

Conclusions: High rates of TB-related deaths were found among enrolled patients with ≥ 24 months of follow-up in an Ethiopian MDR-TB treatment in a larger cohort with severe undernutrition, advanced disease and substantial HIV coinfection. Mortality was associated with profoundly low BMI and due to complications of long-term untreated TB such as respiratory failure and *cor pulmonale*. Our results argue for earlier diagnosis and access to appropriate MDR-TB treatment to diminish advanced lung disease and TB-related sequelae. Additional interventions targeting adverse drug effect management including nutritional supplementation should also be an essential component of MDR-TB treatment programs in resource-constrained settings.

PD-1087-29 Novel treatment regimens for rifampin-resistant tuberculosis: linking specific regimen characteristics to expected population-level impact

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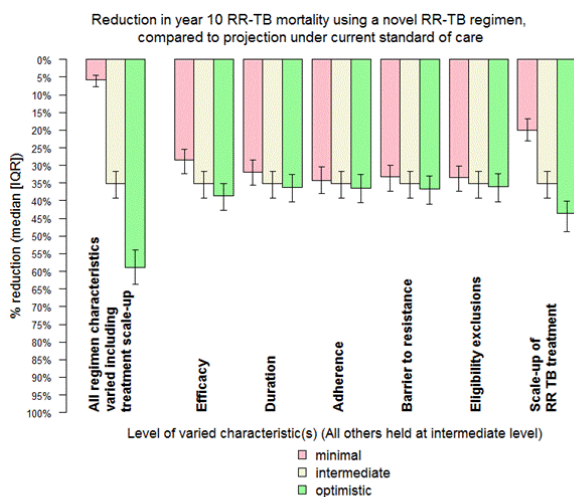
Background: Novel treatment regimens for rifampin-resistant tuberculosis (RR-TB) could improve upon current efficacy, duration, safety, tolerability/adherence, and barriers to emerging resistance. It is useful

to understand which improvements could have greatest epidemiological impact.

Methods: We developed a dynamic transmission model of a multi-strain TB epidemic calibrated to present-day treatment practices, in a representative high-burden population with India's TB and RR prevalences. We introduced a novel RR regimen, improving regimen characteristics individually and in combination. We also allowed for increasing access to RR-TB treatment. We compared the projected impacts of these improvements on RR-TB incidence and mortality after 10 years, relative to continuing current care.

Results: A regimen that moderately improved each characteristic to 'intermediate targets' (Figure) could reduce RR-TB mortality by 35% (95% uncertainty range 26-46%) over 10 years if scaled up rapidly to reach 3/4 of known RR-TB patients. The individual regimen characteristic with greatest population impact was efficacy: Maintaining current efficacy ('minimal target') attenuated the novel regimen's impact on RR-TB mortality from 35% to 28% (95% UR: 20-39%), whereas increasing efficacy further to match current drug-susceptible TB regimens ('optimistic target') improved the mortality impact to 39% (95% UR: 30-51%). Importantly, we found that increasing detection and treatment of RR-TB (which could be facilitated by better treatment options) had greater impact than any intrinsic regimen characteristic; meeting all intermediate targets without any increase in RR-TB treatment uptake lowered the estimated reduction in 10-year mortality to 20% (95% UR: 14-31%). No other individual regimen characteristic affected mortality by more than 5%. Projected impacts on RR-TB incidence were similar.

Conclusions: Developers of novel RR-TB regimens should prioritize improvements in efficacy to optimize epidemiological impact. For other regimen improvements, impact on RR-TB incidence and mortality is tied to the ability of more easily-administered regimens to facilitate more detection and treatment of RR-TB.



Characteristic of novel RR-TB regimen	Efficacy (durable cure among regimen-susceptible patients who complete specified duration)	Duration (Months required to achieve specified efficacy)	Adherence (Reduction of loss to follow up and intermittent nonadherence)	Barrier to resistance (How often novel-regimen resistance arises)	Eligibility Exclusions (Medical or resistance-based contraindications to novel regimen)	Scale-up of RR-TB treatment (Better regimen facilitates increased RR detection)
Modeled values:	76% (~current RR standard of care)	20 months 9 months 6 months	No change (~current RR standard of care) 25% improvement 50% improvement	1 in 10 treatment courses 1 in 20 treatment courses 1 in 125 treatment courses	15% of patients excluded 5% excluded 0% excluded	Current treatment levels Reduce under-treatment of RR by 50% Reduce by 100% (e.g. universal rifampin DST)
Minimal target	88%					
Intermediate target	94%					
Optimistic target						

PD-1088-29 Outcomes for pregnant and postpartum women with drug-resistant tuberculosis and their infants in Belarus

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Background: Tuberculosis (TB) is most common during woman's reproductive years and can affect pregnant women. Belarus is the country with one of the highest level of M/XDR-TB. There are critical knowledge gaps regarding the management and clinical outcomes of M/XDR-TB in pregnant and the postpartum women as well as infant outcomes.

Methods: In this study we analyze clinical course, treatment, pregnancy and infant outcomes in pregnant and postpartum women with drug resistant (DR) TB, diagnosed in Belarus in 2008 - 2013.

Results: Twenty two women (19-41 years) with confirmed DR-TB by DST were included in the study. DR-TB was diagnosed (8 months - 2 weeks) before pregnancy in 17 and (3 months - 1 week) after delivery in 5 women; 8 women were newly diagnosed, 14 were previously treated for TB; 18 had MDR-TB, 2 - XDR-TB, and 2 - poly-DR-TB. There were the following DR-TB treatment outcomes: cure - 5 (23%), treatment completed - 13 (59%), treatment failed - 4 (18%). The following pregnancy outcomes were observed: term delivery - 12 (55%), preterm

delivery - 2 (9%), surgical abortion - 8 (36%; of those 17 with DR-TB diagnosed before pregnancy - 47%). For those with delivery there are the following infant outcomes: healthy newborn - 9, low birth weight - 3, neonatal jaundice - 1, functional immaturity of fetus - 1, stillbirth - 1.

Conclusions: The most important findings are: 1) DR-TB has never been diagnosed during pregnancy (only before and in postpartum period); 2) about half of women with diagnosed DR-TB and pregnancy had surgical abortion. Our study confirmed the need in strengthening collaboration between NTP, obstetrics, neonatology and pediatrics services on the problem TB in pregnancy.

PD-1089-29 First MDR-TB hospital in post-conflict Somali region: outcome and lessons learnt

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Background: Tuberculosis (TB) remains a serious public health problem in the Somali region. In 2011 a World Health Organization survey found multi-drug resistance TB (MDR-TB) in patients with new and previously treated TB, 5.2% and 40.8% respectively. This level of drug resistance is among the highest ever documented in Africa and underscores the magnitude of the region's fragile public health system.

Intervention: The Hargeisa TB hospital MDR-TB centre was set up in 2013 in collaboration with the Somaliland Ministry of Health (MOH), World Health Organization (WHO) and World Vision. The centre consists of 30 inpatient beds in newly refurbished wards. Drug sensitivity testing (DST) on specimens are initially processed using GeneXpert MTB/RIF. Specimens are sent to the National Reference Laboratory in Kampala lab for culture and DST confirmation. All new cases are hospitalized during the initial phase of treatment and follow up care is conducted in peripheral TB centres with DOT. Patients are discharged in the care of voluntary guardians that vouch for them. Peripheral clinics send weekly treatment outcome reports to the hospital.

Results and lessons learnt: To date, a total of 165 patients with MDR-TB from the Somali region and Ethiopia were admitted and started on treatment from MDR-TB. Patients are mostly male (62%) and in the 15-34 age group (65%). Treatment was stopped for 59 (35%) of the patients. Of those, treatment was completed for 54% (32) and 25% (15) were lost to follow-up. More males than females were lost to follow up (10 vs 5) and most are from remote nomadic communities. A total of 12 patients died

during their treatment of which majority were elderly persons with advanced stage of disease.

Conclusions: MDR-TB has emerged as a serious public health issue which is placing a significant burden on an already fragile healthcare system. There is a need to strengthen diagnostics services, improve training, and establish a more coordinated surveillance and case management of MDR-TB patients. More importantly there is a lack of support structure to ensure patient adherence to treatment. The development of extensively resistant strains of TB in the region is a real threat.

PD-1090-29 Multidrug-resistant tuberculosis treatment effectiveness: cohort analysis based on treatment and patient follow-up data

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Background: The prevalence of multi-drug resistant tuberculosis (MDR-TB) in Moscow is one of the lowest in the Russia. Nevertheless, the high population density, significant level of migration and the high proportion of social disadapted persons among TB patients in the megapolis require the special attention to MDR-TB control measures. The high level of 'lost to follow up' (LFU) outcomes among this category of patients, particularly in condition of long-term treatment by the number of anti-TB drugs, creates a problem of assessing the actual patient-based treatment efficiency using the traditional cohort analysis, which deals with 'cases' of treatment, rather than the treatment of patient as a whole, who can have more the one treatment course during 1-3 years before treatment completion. In Moscow, for the analysis of the effectiveness of treatment of MDR-TB patients are used annual cohorts, based both on the data on treatment courses (TCD) and data of follow up to MDR-TB patient (PFD) from the time of its registration in the cohort, up to the date of final outcome, which reflects the effectiveness of treatment for separate MDR-TB patient in a whole.

Methods: Cohort of 425 MDR-TB patients, registered in 2013 in Moscow, was evaluated by 2015 based on TCD and PFD information.

Results: The 2013 cohort, covered 82.5% of all MDR-TB patients registered in Moscow, including 14.6% of XDR-TB, 12.7% of TB-HIV, 26.6% new TB cases with 9.7% XDR-TB and 20.2% of TB-HIV. Treatment outcomes, calculated based TCD: Total cohort: treatment success - 45.9%, failure - 14.1%, died - 16.9%, LFU - 22.8%. New MDR-TB patients' cohort: treatment success - 66.4%, failure - 5.3%, died - 14.2%, LFU - 14.2%. Treatment outcomes, calculated based on PFD: treatment success - 45.9%, died - 18.1%, failure including incurable chronic TB

patient receiving the symptomatic treatment - 7.8%, reregistration on new MDR-TB course in 2014-2015 - 11.1%, moved to another area with no treatment data - 13.9%, and 'real' LFU - 1.9% (95%CI 0.8 - 3.7).

Conclusions: Patients-based cohort analysis, as well as treatment courses-based cohort analysis, are important for a comprehensive and efficient monitoring of MDR-TB treatment.

PD-1091-29 Overview of the Programmatic Management of Drug Resistant TB Program in Khyber Pakhtunkhwa, Pakistan

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Background: Multidrug-resistant tuberculosis (MDR-TB) is posing a great threat to global TB control. Pakistan ranks 4th among 27 MDR-TB countries. KP is one of the Provinces of Pakistan, where DR-TB is treated under PMDT.

Objective: The aim of the study is to have an overview of the PMDT Program in KP. We retrospectively reviewed data at different PMDT centers in KP from 1st Q 2012 –4th Q 2015.

Methods: To control the increasing rate of DR-TB in KP, PTP KP stepped up & started managing M/XDR-TB in 2012 with the support of Global fund. Four PMDT centers have been established in KP. The enrolled DR TB patients at these centers were not only provided free second line drugs but also social support and travelling allowance on monthly visits.

Results: Total of 1166 patients were enrolled in four centers and among them 778 (66.7%) were MDR. Among enrolled patients 523 (44.9%) were male and 643 (55.1%) female. This study included all those patients who were registered up to December 2013 and were completed their treatment. A total of 521 patients were registered during this time, out of which 511 were completed their treatment and were included in this study. Among these patients 28 were Rif resistant on Xpert testing and not declared MDR-TB on culture, out of which 23 declared cured and 5 died. Four were Mono DR-TB, of which completed 1, cured 1 and 2 were died. Among completed patients 14 were PDR-TB out of which 10 declared cured, 2 died and 2 was failed. Four hundred and forty three were MDR-TB, of which 323 (72.9%) has successfully completed treatment. Unsuccessful were 95 (27.1%) (Died = 71, Failed = 23, Lost to follow up = 1) and 10 were still under treatment. Among these 44 were XDR cases, out of which 29 completed their treatment while 15 are still on treatment. Among

completed, cured were 6 (20.7%), Died=13 (27%), failed=7 (24.1%), lost (3.4%) and transfer out were 2 (6.8%).

Conclusion: Multidrug-resistant tuberculosis is an emerging challenge in Pakistan. There is a need to invest in improving the capacity of the TB Program to detect and manage DR-TB.

49. Mental health, diabetes and other comorbidities in TB

PD-1092-29 Impact of concurrent mental health illness on TB treatment outcomes: a case of Butabika Hospital in Uganda

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Background: Butabika National Mental Health Referral Hospital accounts for 2% ($n=8,000$) of all the TB cases annually notified by Kampala Capital City. Butabika has an average annual treatment success rate (TSR) of 75% as compared to the overall TSR of 80% in Kampala. We sought to determine the impact of concurrent mental health illness on TB treatment outcomes.

Methods: We conducted retrospective mental illness based comparative bivariate and multivariate analysis of 225 patients notified for TB treatment in the period of July 2013 - June 2015 at Butabika hospital. Factors included were: Treatment-outcome, Age, HIV-Status, cotrimaxazole preventative therapy (CPT)-Uptake, directly observed treatment (DOT), and antiretroviral therapy (ART)-Uptake.

Results: 62% of the patients were male. 30% (69) of TB cases were also diagnosed to have mental illness. 51% percent (35) of the mentally ill patients were also HIV-positive with 97% (34) on CPT and 49% on ART (17). Only 49% (34) of the patients with mental illness were found to have successfully completed TB treatment compared to 78% of the patients without mental illness. A comparison of odds ratios showed that patients with mental illness were: 4 times less likely to complete treatment (OR 3.66, $P=0.000$), 3 times less likely to cure for pulmonary bacteriologically confirmed (P-BC) TB (OR 2.7, $P=0.128$), 3 times more likely to die during treatment irrespective of HIV status (AOR 2.7, $P=0.01$) and more than twice as likely to be lost to follow up (OR 2.5, $P=0.057$). Patients with psychosis were 6 times more likely to die on treatment (OR 6, $P=0.02$) compared to patients with other mental illnesses. Among mentally ill patients, pulmonary clinically diagnosed

(PCD) and extra pulmonary (EP) TB were 5 times less likely to complete treatment compared to P-BC (OR 5.4, $P=0.04$).

Conclusion: Mental illness is associated with unsuccessful completion of tuberculosis treatment. Further studies with larger samples should focus on increasing our understanding of the possible biological and social factors responsible for this association, as well as addressing the knowledge gap in provision of care for mental health patients treated for TB.

PD-1093-29 Burden of comorbidities and social determinants of health among tuberculosis patients in Carabayllo, Peru

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Background: A tuberculosis (TB) patient management program called TB Cero was established in Carabayllo, a district in the north of Lima. Through strengthening and complementing the existing health system, TB Cero sought to support patients in the management of their TB as well as their other needs. The objective of this analysis was to describe the burden of comorbidities and social determinants of health in patients with TB at the time of treatment initiation.

Methods: We used data collected for the monitoring of the TB Cero program. As part of TB Cero, all patients who initiated treatment in the 9 health facilities of Carabayllo during 14 September, 2015-11 March, 2016 were identified. All patients received an HIV test as part of routine procedure. TB Cero offered a glycosylated hemoglobin test for diabetes screening. As part of TB Cero, a mental health team and a social protection team visited patients in their homes to assess each patient's needs. Based on the results of all of these evaluations, TB Cero referred patients for further medical attention and/or provided direct support as necessary.

Results: TB Cero identified 135 patients who initiated TB treatment. Eight (6%) patients had a positive HIV test result. All of them already knew their HIV status, but only four (50%) were receiving antiretroviral therapy at the time of TB diagnosis. Of 72 (53%) patients who received a test for glycosylated hemoglobin, 8 (11%) had elevated levels of glycosylated hemoglobin indicating diabetes or pre-diabetes; of these, only 3 (38%) knew about their condition. Of 98 (73%) patients evaluated by the mental health team, 47 (48%) were diagnosed with a mental health condition. The social support team assessed 86 (64%) patients for unmet basic needs. Of these, 50 (58%) required some form of social support.

Conclusions: Among TB patients in Carabayllo, we

found a substantial burden of medical comorbidities, particularly mental health conditions, as well as unmet basic needs. An analysis to determine whether TB Cero's integrated approach to managing TB patients' various medical and non-medical needs can improve treatment outcomes is planned.

PD-1095-29 Risk factors for tuberculosis going beyond HIV: a case control study in Western Kenya

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Background: Tuberculosis (TB) control efforts in Sub-Saharan Africa have been focused around curbing HIV related TB. However recent evidence indicates growing importance of Non-Communicable diseases (NCDs) as TB risk factors in developing countries. While HIV remains an important driver of TB in Kenya, 67% of cases are not HIV related suggesting the need to identify and address other drivers of the epidemic. This study was conducted to determine the role of NCD in the TB epidemic.

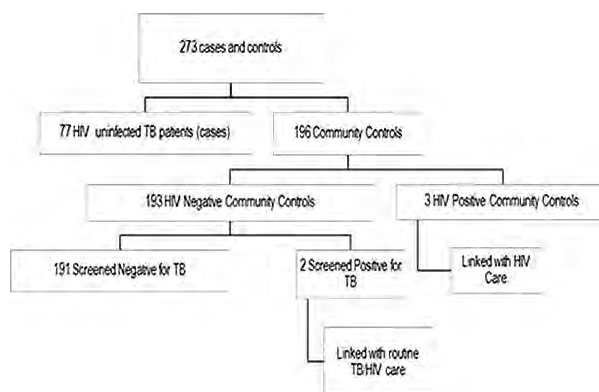
Methods: This was a case-control study conducted in five facilities in rural Western Kenya from September 2015 to January 2016 among consenting adults aged 18 years or older. Cases were registered TB patients at the time of study, while controls were individual living in the same community as cases and screened negative for TB. HIV infected cases and controls were excluded. Cases were systematically selected from facility TB registers while controls were randomly selected from the community. Data on exposure variables; alcohol consumption, cigarette smoking, malnutrition and diabetes mellitus (DM) were collected on ODK platform and analyzed using Stata. DM was defined as fasting blood sugar (FBS) ≥ 126 mg/dl or RBS of ≥ 200 mg/dl and malnutrition as body mass index ≤ 18.5 Kg/M². Sample size was calculated using Kelsey formula.

Results: A total of 77 cases {mean age: 32 years (SD: 10), 65% males} and 191 controls {mean age: 35 years (SD: 13), 59% males}. Ten cases of DM (80% new) cases were identified among cases and 7 (100% new) among controls. Tuberculosis was independently associated with DM (AOR_{MH}=3.30, 95%CI=1.13 - 9.68; P=0.0001), cigarette smoking (AOR_{MH}=2.82, 95%CI=1.15 - 6.88; P=0.0001) and malnutrition (AOR_{MH}=14.54, 95%CI=6.19 - 34.13; P=0.0001).

Conclusions: Diabetes, Cigarette smoking and malnutrition play a significant role in the epidemiology of TB. Majority of DM cases among TB patients remain

undiagnosed. Reconfiguration of primary healthcare to integrate TB, HIV and NCD control programs is recommended.

Figure Procedure for selection of cases and controls



PD-1096-29 Impact of diabetes mellitus on treatment outcome of multidrug-resistant pulmonary tuberculosis

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Background: Multiple studies have indicated that patients of pulmonary tuberculosis with diabetes mellitus may experience poor outcome. Emergence of Multidrug Resistant-TB has further complicated the situation as its management may be challenging in presence of diabetes. There is a paucity of data on effect of diabetes on outcome of MDR-TB in Indian context. The study aimed to assess the effect of Diabetes Mellitus on mean time for sputum culture conversion and treatment outcome in patients of Multidrug Resistant Pulmonary Tuberculosis.

Methods: The present observational cross-sectional study was conducted at Drug Resistant-TB centre, S.R.N. Hospital, M.L.N. Medical College, Allahabad. 144 diagnosed patients of MDR-TB treated with Category IV DOTS, were retrospectively analysed for the effect of DM as a comorbidity on their outcome on treatment completion. The diagnosis of Diabetes Mellitus and treatment outcomes were defined as per WHO guidelines.

Results: Out of 144 MDR-TB patients, 13 (9.03%) had co-existing Diabetes Mellitus. Patients having MDR-TB with Diabetes had longer sputum culture conversion time (131.4 \pm 40.99 vs 118.72 \pm 41.54 days, P=0.358) compared to MDR-TB patients without diabetes. They also had 2.75 times higher

odds of death than patients in non-diabetic group (53.85% vs 30.47%, 95% confidence interval [CI] 0.869 to 8.717). Non-diabetics had 1.84 times higher odds of culture negativity at 6 months (54.26% vs 38.46%, CI=0.57 to 5.91) and 1.73 times odds of successful treatment (44.53% vs 30.77%, CI=0.51 to 5.91) compared to diabetic patients. 12.5% patients defaulted on treatment in non-diabetic group while diabetic group had no default. 15.38% patients failed treatment in diabetic group compared to 12.5% in non-diabetic ($P=0.667$). Outcome of 3 patients was not known since they were transferred out.

Conclusions: Diabetes Mellitus as a comorbidity was associated with longer culture conversion time, decreased success rate, higher treatment failure and higher death rate among patients of MDR-TB, but the results were not found to be statistically significant, which may be due to small sample size in the MDR-TB with diabetes group.

PD-1097-29 Effect of type 2 diabetes mellitus on the clinical and paraclinical presentations of pulmonary tuberculosis in North-Eastern Iran

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Background: Diabetes mellitus (DM) is a known risk factor for tuberculosis (TB), and with the increasing prevalence of type 2 DM in less developed regions, many patients with TB will have concomitant DM. Presently, little is known about the effect of DM on the clinical presentation and sputum smears of TB.

Methods: In Golestan Province, 457 patients with pulmonary TB were screened for DM and Results Clinical characteristics and sputum smears were compared between patients with TB who had DM and patients with TB who did not have DM.

Results: DM was diagnosed in 17.5% of patients with TB and was associated with older age and a greater body weight. On presentation, diabetic patients with TB had more symptoms and had evidence of more-severe TB in DM with dyspnea (71.2% vs 56.2%, $P=0.009$) with fatigue and fever. Results of sputum microscopic examination was more often positive in diabetic patients (19.2% vs. 12.9%).

Conclusion: DM seems to have an effect on severe clinical presentations of TB. DM may be influenced underlying mechanisms for the different response to treatment in diabetic patients, then TB must be explored. Screening for DM and subsequent glycemic control may improve severe pulmonary TB and the outcome of TB treatment.

PD-1098-29 Indicators of acute phase reaction in patients with pulmonary tuberculosis combined with diabetes mellitus

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Aim: To compare the level of acute phase reactants (APR) in the blood serum of patients with pulmonary tuberculosis, combined with diabetes mellitus (DM) and without it.

Methods: We studied level of APR in blood serum of 52 patients with pulmonary TB combined with DM. The comparison group consisted of 76 patients with pulmonary TB. Control group consisted of 49 healthy volunteers. The groups were matched by age and sex. Concentration of CRP, α_1 -AT, Hp and F were determined using immunoturbometric methods, SAA by ELISA.

Results: It was found that the level of SAA was increased in vast majority patients of both compared groups (97,8% in patients with DM and 98,7% in patients without DM). On the other hand, CRP is recognized as a classic indicator of systemic inflammation, was increased in the majority of patients without DM and twice as less in patients with DM (80,3% and 43,1% respectively; $P<0,01$). The level of α_1 -AT was increased in 84,5% of patients with DM and in 68,5% of patients without DM. The levels of Hp and F increased with almost same frequency in both group of patients. Concentration of SAA in patients without DM increased more significantly compared to patients with DM ($141,7 \pm 3,8$ and $106,1 \pm 13,7$ respectively; $P<0,02$). Similar changes were found in the study of the concentration of CRP ($41,7 \pm 2,8$ and $28,5 \pm 5,1$ respectively; $P<0,01$). The level of α_1 -AT ($2,2 \pm 0,1$ and $2,4 \pm 0,09$, respectively) and Hp ($1,6 \pm 0,1$ and $1,77 \pm 0,14$, respectively) in both groups did not differ significantly. The level of F in patients without DM, significantly higher than that of the patients in the comparison group ($4,4 \pm 0,1$ and $4,1 \pm 0,1$, respectively; $P<0,05$).

Conclusions: Increasing the levels of APR suggest about the presence of systemic inflammatory response (SIR) in both groups of patients. However, the SIR in patients with tuberculosis combined with diabetes was less pronounced, which was probably associated with reduced production of proinflammatory cytokines, initiating the synthesis of APR.

PD-1099-29 Mental disorders among new cases of tuberculosis in Brazil

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Background: Brazil records about 70 000 new cases of tuberculosis (TB) per year, and among these cases are people with mental disorders. Mental disorders may influence in the control of tuberculosis, particularly in treatment adherence. These disorders can contribute to loss of follow up of treatment, irregular treatments or to failures of treatment and, therefore, it collaborates to emergence of drug-resistant tuberculosis (TBDR). This study aims to analyze the mental disorders among new cases of tuberculosis in Brazil.

Methods: This is a descriptive study comprehending 1,438 new cases of tuberculosis with mental disorders as comorbidity, diagnosed in Brazil in 2014. Data were obtained from the national information system for notifiable diseases. The variables analyzed were sex, age, race and Federated Unit of notification, area of residence, mental illness, sputum smear, sputum culture and HIV testing, as well as evolution data and outcomes. Only new cases of the comorbidity tuberculosis and mental disorders were included in the analysis.

Results: In 2014, in Brazil, 2.1% of new TB cases occurred in person with some mental disorder. 67.5% of them were males, in the age group 20-59 years (79.8%) and black (57.2%). The most of comorbidity cases were living in urban areas (71.0%) and most prevalent in São Paulo (17.2%), Rio de Janeiro (12.2%) and Pernambuco (10.9%). About diagnostic tests: 70.0% did sputum smear, 20.5% did culture exam, 68.9% of the cases were tested to HIV and 12.6% were TB-HIV coinfecting. 54.0% were followed with directly observed treatment, and about outcomes, 67.1% reached cure, 11.0% lost to follow-up, 5.4% were transferred and 0.7% were or became TBDR.

Conclusions: This study showed the presence of patients with mental disorders in the new cases of tuberculosis in Brazil. The results points that it is necessary expand the training for health professionals to improve care for people with mental disorders as a strategy to upgrade patient-centered approach and create opportunities toward TB cure, mainly preventing the emergence of TBDR cases.

PD-1100-29 Xpert® MTB/RIF assay for pulmonary tuberculosis diagnosis in patients with pre-diabetes mellitus and diabetes mellitus

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Background: Diabetes Mellitus (DM) leads to increased risk of tuberculosis (TB), more severe disease, and higher incidence of death, failure, and/or relapse. Xpert® MTB/RIF is highly sensitive and specific for diagnosis of TB and rifampicin resistance, however data suggest that sensitivity may be lower among patients with HIV and limited data are available among patients with pre-DM and DM. We sought to assess the sensitivity/specificity for TB among patients with pre-DM and DM and suspected TB.

Methods: A prospective study was conducted between December 2013 and 2015 among adults suspected to have pulmonary TB (PTB) at BJ Government Medical College, Pune, India. All PTB suspects underwent two sputum smears, cultures and Xpert® MTB/RIF assays and underwent HbA1c and fasting blood sugar (FBS) testing. DM was defined as HbA1c >6.5 or fasting blood sugar (FBS) >126 and pre-DM was defined as HbA1c of 5.8- < 6.5 or FBS between 110 and 126. We assessed the sensitivity/specificity of the Xpert® MTB/RIF assay for TB among adult PTB suspects with or without pre-DM or DM using positive TB liquid sputum cultures as gold standard.

Results: 766 patients were screened for PTB; DM and pre-DM was diagnosed in 121 (17%) and 208 (29%) patients respectively. The Xpert® MTB/RIF assay was positive among 367 (48%) patients overall; 85 (25%) and 106 (32%) with DM and pre-DM, respectively. Compared to gold standard of TB cultures, Xpert® MTB/RIF assay sensitivity was 97% overall; as compared to 96% in patients with TB alone, sensitivity was 100% and 97% among DM ($P=0.06$) and pre-DM patients ($P=0.68$), respectively. The specificity of assay was 95% overall; specificity was 97% and 98% among patients with DM and pre-DM, respectively as compared to 97% in patients with TB alone ($P>0.20$).

Conclusions: There was no observable difference in sensitivity or specificity in Xpert® MTB/RIF among DM, pre-DM or TB alone. The sensitivity and specificity was very high, providing evidence of its utility among pre-DM and DM populations.

50. Media communication: for or against tobacco use strategies

PD-1101-29 Study on how media influence (impact) on tobacco promotion could be reversed or corrected

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Background and challenges to implementation: Tobacco use has been the leading preventable cause of death and disease and per day 60 to 70 persons are dying in Sri Lanka. It is proven that, this risky behavior is often initiated during childhood and adolescence. They are often influenced by Television, movies, advertising, and by peer pressure.

This study was to experiment how and what type of methods could be used to correct and reverse the media influence on tobacco promotion.

Intervention or response: 260 students were addressed in 3 locations within 9 months project period. The discussions with them were mainly based on how media influences create a positive image on tobacco and smoking. A pre test was carried out prior to the discussion to assess the media literacy on tobacco promotion and a post test was done after the intervention.

Training and follow-up discussions were supplemented by educational materials which were: media analyze chart, Leaflets and Puzzles games. Public awareness campaigns were also conducted.

Results: 81% of children were able to mention harm caused by smoking and children were getting used to respond to the people who smoke. Children were able to explain the harm caused by smoking like unattractive look, the bad smell, and unpleasant look.

67% of the children who participated in the program were aware on how movies, music, TV, Internet, News Papers and Magazines influence the minds of children. Children are aware on which media channel, particular programs and the persons who promote smoking through the media. They had done the media analyze sheet which was provided by ADIC and shared the results with their friends.

Children and the community were reacted as pressure groups to create a child friendly media environment through the motivation of the children.

Conclusions and key recommendations: It is possible to create an environment where targeting children through mass media promotion on tobacco and smoking will be less. Because the methods used by the companies could be identified by the children such

as strategies, monitor the extent, the impact and respond appropriately.



PD-1102-29 Ban on tobacco advertising: an absolute public health gain in Jakarta

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Background and challenges to implementation: Enforce bans on tobacco advertising, promotion and sponsorship is one of the six component of MPOWER strategy. Tobacco advertising is a powerful lure to initiate people to start smoking and targeted woman and young generation. Banning tobacco advertising in Jakarta will contribute to protect 12 million people and as a milestone for TAPS ban implementation at sub national level in Indonesia. In 2015, Jakarta has 185.773 advertising, which consist of 162.459 outdoor advertising, 23.252 indoor advertising, and 62 rooftop advertising. 4.861 of them are tobacco advertising. In Jakarta, 25% higher tax applied for tobacco advertising, this argument was being used by tobacco industry front groups to challenge its regulation.

Intervention or response: Technical assistance in advocacy, drafting, conduct high level meeting with

government officials and facilitating on monitoring and enforcement of the law.

Results and lessons learnt: In 2014 Jakarta Law to ban tobacco advertising was adopted. The provision of the law mandates the Governor to define areas banned from tobacco advertising, which in principle gives rooms for the government to apply the comprehensive ban. An intensive advocacy to the local government was contributed on the adoption of Governor Regulation No. 1/2015 and 244/2015, tobacco advertising now ban in the entire territory of Jakarta.

A unique and intensive collaboration with Tax Office and Civil Police was managed to monitor and enforce the law. Monitoring started with identifying tobacco advertising location and expiry dates. A SMART target was set to achieve Jakarta 100% tobacco billboards free by March 2016. Regular monitoring and evaluation with Tax Office and Civil Police was conducted to identify current status of removal. As a result of our intensive advocacy and after a year of intensive enforcement, 4861 tobacco billboards were removed. Jakarta now declared as tobacco billboard free city.

Conclusions and key recommendations: Civil society support is an effective strategy to support local government to provide an adequate tobacco control legislation for the people. Monitoring and enforcement are the key success of tobacco advertising ban. It is an absolute public health gain. 12 million people especially young generation is now protected.

PD-1103-29 Beyond the school gate: bombarded by cigarette advertising

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Background and challenges to implementation: Approximately 70 percent claims to start smoking due to the influence of advertisements. Exposure to TAPS from young age increases positive perception of smoking and desire to smoke. By law, schools are supposed to be smoke-free, cigarette sales and TAPS. However, tobacco companies are using a variety of tactics, from billboards, to indirect marketing tactics like painting buildings with brand's colors. They are still able to advertise and sell cigarettes outside of the school gates where children are immediately ambushed by advertisements. Cigarette advertisements were found in 85 percent of the school areas.

Intervention or response: The teachers and principals who have many tobacco advertising around their schools were shown an evidence of the bad effect of tobacco advertising, how it could influence students to smoke and those advertising were placed around

schools and attacking their students indirectly. The 8 school groups in Jakarta and Bandung agreed to take down the tobacco advertising around schools. We educate their students about the harms of cigarette and its advertisement. After that, the students came to sub-district office to work together to clean up school's environment from tobacco advertising.

Results and lessons learnt: The students, teachers, sub-districts, civil polices, and community worked together to clean up the tobacco advertising around their schools and replace it with anti-smoking banners. The kiosk owners have been educated by the students and they did not mind to replace the advertising. It took 6 months for all community to take action. The constraints of this activity is timing. Besides we need to always stick to the school groups, school's holidays and final exam are a challenge for approaching schools.

Conclusions and key recommendations: Although some cities have regulation to ban outdoor advertisements, but our children are not yet fully protected from the tobacco industry's tactics. This statements were agreed by the 8 intervention school who have taken down the advertising. This result concludes with the following recommendations: 1. Local and national governments must implement total bans of TAPS; 2. Concerned group take action to make school environment free of TAPS.

PD-1104-29 An analysis of online marketing of bidi smoking tobacco in international markets

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Background and challenges to implementation: Bidi is one of the most common form of consuming smoking tobacco in India. Bidi is hand rolled by wrapping traditional tobacco in tendu leaves (*Diospyros Melanoxylon*). Smoking bidi is quite common in rural parts of India because of its low price. Bidi industry in India till now concentrated on domestic rural market but now new strategies are being adopted for global markets. This analysis was done in order to understand the strategies of Indian bidi companies for international marketing through on-line medium.

Intervention or response: Analysis of content of the websites of major bidi manufacturing companies of India on the basis of 4Ps of marketing ie. Product, Place, Price and Promotion. The analysis was done on the basis of their product types offered, other business interests, promotional strategies, pricing strategies etc.

Results and lessons learnt: Most of the bidi companies are using online presence to market products in other countries, flavoured bidis are available in menthol, clove, chocolate, pineapple etc flavours. Some companies promoted bidi as having less

tobacco content than cigarette and promoted that tendu leaves used in bidi having herbal properties, bidi made of organic tobacco was also promoted, customer testimonials were displayed in attractive manner having customers from various parts of the world advocating about bidi smoking experience, some companies were promoting designer matchbox in the name of bidi brands, less pricing of bidi is promoted to attract more customer as smoking bidi cuts smoking expenses, some companies have also used photographs of celebrity smoking bidi.

Conclusions and key recommendations: The analysis of the websites shows that bidis which were till now a product of rural India is being marketed all over the world and it may result into shifting of trend from cigarette to bidi in developed countries. Websites are becoming very effective tools for bidi companies for international marketing. Chances of increasing the prevalence of tobacco consumption is very high as bidi becomes a new and innovative product for current tobacco users and also a cheap attractive smoking agent for new users.

PD-1105-29 Tobacco advertisements, promotion and sponsorships in India: business of lies and deception continues

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Background: Tobacco industry has been using all possible tools to market their deadly products globally and earn profits at the expense of public health, lost lives, and untold sorrow. In India, newer and manipulative tactics are being used by tobacco industry, circumventing the Indian tobacco control law (COTPA) and carrying the business of lies and deception. It is important for tobacco control advocates and law implementers to have an understanding how tobacco companies market their deadly products. This information is important in designing tobacco control efforts and get better prepared to counter the industries tactics. The researchers did the present study with the objectives to keep a track and monitor tobacco industry tactics and overview range of the ongoing tobacco advertising promotion and sponsorship (TAPS) violations in India.

Methods: Researcher did the newspaper scans, market survey and company's website search in 2013, 2014 and 2015. The marketing materials at point of sale (PoS) were also analyzed.

Results: Tobacco industry is utilizing PoS as a strategic location for carrying out TAPS in India. Companies are paying retailers to display the advertisement billboards and tobacco products are placed strategically to give an ambience of power walls. Near all cigarette brands are offering price discounts and encouraging single cigarette sales.

Contests, giveaways and coupons for gift catalogs are other gimmicks in practice. Though direct advertisements are banned in India but industry is carrying out surrogate advertisements as trademark diversification and brandstretching especially in print and outdoor media. Industry has been successful in product placement in movies and promoting tobacco through film stars. Tobacco use in bollywood movies and on television is portrayed as fun, exciting, rebellious and symbol of success. As part of the image building exercise, most of the tobacco companies are doing CSR activities. The industry effectively and discreetly is using social networking sites.

Conclusions: Tobacco industry in India is carrying out aggressive advertising and promotion and sponsorship campaigns to glamorize its deadly product through indirect advertising and deceitful tactics. There is an urgent need to enforce legislation (COTPA) to contain all common types of TAPS violations in India.

PD-1106-29 Advancing towards tobacco-free Chattisgarh using communication as a tool to deter people from chewable forms of tobacco

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Introduction: In Chattisgarh tobacco is consumed mainly in the form of bidi smoking and in smokeless form such as chewing tobacco and Gutka.

Following findings were found:

- Current tobacco use in any form: 53.2% of adults; 63.9% of males and 41.6 % of females.
- Current tobacco smoking: 12.6% of adults; 20.9 % of males and 3.7% of females.
- Current users of smokeless tobacco: 47.2% of adults; 52.5% of males and 41.6% of females.

Interventions: Mass-reach health communication interventions can be powerful tools for preventing the initiation of tobacco use, promoting and facilitating cessation, and shaping social norms related to tobacco use. They are particularly helpful in decreasing the prevalence of tobacco use; increasing cessation and use of available cessation services such as quitlines; and decreasing initiation of tobacco use among young people. Media campaign research and evaluations have shown that advertising that elicits negative emotions through graphic and personal portrayals of the health consequences of tobacco use is especially effective in motivating smokers to quit.

Effective health communication interventions and countermarketing strategies employed include:

- Paid television, radio, out-of-home (e.g., billboards, transit), print

- Media advocacy through public relations often timed to coincide with holidays, heritage months, and health observances,
- Health promotion activities,
- Innovations in health communication interventions such as online video, mobile Web, and smartphone and tablet applications (apps),
- Social media platforms such as Twitter and Facebook, facilitated improvements in message development & dissemination.

Results:

- 34.4% of current smokers and 35.0% of users of smokeless tobacco planned to quit .
- Adults who noticed any advertisement or promotion: 32.0% for cigarettes, 77.8% for bidis and 81.4% for smokeless tobacco.
- Current users of the following tobacco products who thought about quitting because of a warning label: 32.2% for cigarettes, 14.2% for bidis, 36.1% for smokeless tobacco.

Conclusion: When planning and developing a mass-reach health communication campaign, the most critical considerations are that the messages resonate effectively with each priority audience. Taking into account these considerations should ultimately help that the messages lead to meaningful changes in tobacco related knowledge, attitudes, and behaviors.

PD-1107-29 Letter to editor as an innovative tool of media advocacy for tobacco control

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Background and challenges to implementation: Print Media always played an important role in generating awareness and advocating for policy change and influencing decisions in support of the public. It is very difficult to get earned media coverage in print media in a country like India. Most of the social issues are neglected in media due to lack of news space. Letter to editor is an innovative and effective means of raising a social issue in print media.

Aim: The aim of the intervention was to get space in print media and generate awareness about the various issues related to tobacco control.

Intervention or response: Media advocacy is done in one of the leading Newspaper 'Free Press' of Madhya Pradesh state of India and letter to editor were sent to the editorial section of the newspaper on the most recent and relevant issues related to tobacco control. The process was carried out for a duration of 9 months (April 2015-Dec 2015). The results were analyzed on the basis of content of letter, issue raised, amount of earned media coverage.

Results and lessons learnt: During the period a total of 11 letter to editors published in editorial page of

Free Press Newspaper. Topics ranging from role of parliamentarian in tobacco control, inclusion of tobacco in Juvenile Justice Act of India, illicit trade, tobacco industry interference, establishment of tobacco testing labs, E cigarettes, raising taxes, stronger pictorial warning, integration of TB and Tobacco Control program, regulation on low cost tobacco products, tobacco control as development issue etc were covered. The total space occupied by the letter to editor was approximately 500 sq cm and a total of 1600 words were published in editorial page. As letters are published in editorial page of the newspaper so its readership among policy makers and decision makers is much high as compared to other news item.

Conclusions and key recommendations: Raising the issue in editorial page of the newspaper is effective in getting earned media coverage and influencing policymakers, top level decision makers, elected representatives, editor and other intellectuals for their increased involvement in the field of tobacco control. Letter to editor should be used for effective media advocacy.

PD-1108-29 Effectiveness of complementing paid social media with organic social media

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Background: As more consumers turn to the internet for health related information, health organizations have begun to use social media as a tool for connecting with the public. Unlike for-profit businesses, which sell a product or service, health organisations market a cause or mission, which requires clear and effective communication of the organization's goals and needs. Paid and earned social media may be used complementarily to increase social media campaign investment, but a careful analysis of how these work together is required. Hence, the objective of this paper was to assess the effectiveness of synergizing paid social media activity with organic activity and its effectiveness in generating engagement with the targeted audience. In December 2015, the Government of Maharashtra in India launched a 4 week traditional mass media campaign to warn people about the deadly effects of secondhand smoke. A social media campaign was initiated to amplify the reach of the MMC and provided a test of our hypothesis.

Method: Every day two posts were made which were descriptively analyzed over a period of two months. Two of the 14 posts in a week were boosted keeping in mind the target of the post. To understand the effectiveness of the paid posts and to monetize each interaction, the campaign was evaluated based on

Cost Per Million (CPM) model of Facebook- how much money is spent to get 1 million impressions.

Result: The campaign video had more than 32 000 views. Around 600 000 people saw the posts more than 700 000 times and more than 25 000 times people were engaged. By spending USD 1143, we engaged 4,76,388 people on our Facebook page and posts in a period of two months, so by spending USD 1, we were able to engage 417 people. Further analysis is currently underway to calculate the Cost per Acquisition and Cost per Engagement.

Conclusion: Social media has provided the nonprofit world, offering a valuable way to engage audiences and promote an organization's cause. This paper demonstrates how even small investments in social media can be achieve significant reach, when targeted appropriately and synchronized with traditional mass media campaigns.

PD-1109-29 Trend analysis of pan masala advertisements in print media

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Background and challenges to implementation: Article 13 of FCTC and section 5 of Indian Tobacco Control Act prohibits indirect advertisements of tobacco products. Pan masala which is a mixture of areca nut with various flavoring agents is getting more popular because tobacco users mix pan masala with tobacco. Pan masala sale is increasing with the ban of gutkha (mixture of pan masala and tobacco) in India. The study was carried out to understand the trend of Pan Masala advertisements in print media in Madhya Pradesh state of India.

Intervention or response: The study conducted for 2 months each in year 2015 and 2016. Advertisements were observed in the month of Jan-Feb 2015 and Jan-Feb 2016. Pan Masala ads were tracked in Indore edition of leading newspaper of India. Comparison was made for both the time periods. The data was analyzed on the basis of space occupied, number, brands and frequency of the advertisements.

Results and lessons learnt: There was a reduction of 36% in number of ads appeared during the period (14 in year 2015 and 9 in year 2016). 14.5% reduction was also observed in amount of space occupied by the ads, a total of 4388 cm² space was occupied in year 2015 and 3750 cm² space was occupied in year 2016. A total of 4 brands advertised in 2015 while in 2016 only 3 brands were advertised. A single brand was advertised 70% of the times in 2016. Result also showed that during the period no new brand was launched through print media. Celebrity endorsement was seen in 36% ads in 2015 but no celebrity endorsement was seen in 2016 in print media advertisements.

Conclusions and key recommendations: A negative

trend in pan masala advertisements during the period means that policy level interventions regarding ban on indirect advertisements of tobacco control are working in print media. If more stringent action will be taken than indirect advertisements can be reduced in print media.

PD-1110-29 Can social media change behaviour as part of a synergised tobacco control communication strategy? Message pre-test findings from Bangladesh

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Background: Currently, there is conflicting and limited evidence for the efficacy of social media to achieve behavioural outcomes for tobacco control and other health programs. This is particularly so in LMIC settings with large populations and exponential growth in internet usage.

Methods: A qualitative study design was embarked upon to pre-test social media pages linked to a national, tobacco-pack pictorial warnings, communication campaign, to be implemented on mass media channels across Bangladesh. Two social media options were designed to include information on the pictorial warnings as well as quit tips and referrals for tobacco users. Eight focus group discussions were conducted for the pre-test, with male and female tobacco users in urban and rural settings of Bangladesh. Components of the site were reviewed including: Graphic health warnings and cessation pages, videos of personal testimonials from tobacco victims related to pack warnings and messages from respected opinion leader clinicians.

Results: Focus Group findings identified a high likelihood by respondents to access the site, or refer tobacco using friends and family members to the quit pages. Responses to testimonials appearing on the webpages identified that the messages had high impact on intentions to make a quit attempt or talk to others about quitting. Respondents also identified their appreciation of quit tips support and referral options. Additionally, barriers and benefits analysis provided insights for design modifications to optimise social media approaches and improve communication campaign synergies.

Conclusions: Pre-testing of social media interventions can provide valuable insights on the optimal design, message content and key components to successfully engage audiences, with the potential to also affect changes in attitudes, intentions and cessation behaviours.

51. Drug resistance assessment: methods, feasibility and results

PD-1111-29 Feasibility analysis of rapid diagnostic tools for drug-resistant tuberculosis in Bangladesh

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Background: Under detection of multidrug resistant (MDR) tuberculosis (TB) is a major concern for many of the high burden TB countries around the world. In a country like Bangladesh which ranks 10th among the high MDR-TB burden countries, rapid and accurate diagnosis of MDR-TB is a great challenge towards a successful TB control program.

Methods: Under a nationwide drug resistant TB surveillance study which included 14 hospitals from 12 districts of Bangladesh, sputum samples were collected from newly registered smear positive TB patients following a systematic sampling strategy. Collected sputum samples were subjected to culture and drug susceptibility testing (DST) in both solid (Lowenstein-Jensen or L-J) and liquid (Mycobacteria Growth Indicator Tube or MGIT) media, Line Probe Assay (LPA) and Xpert MTB/RIF (Xpert) assay. The objective was to compare the rapid diagnostic tools with the gold standard L-J culture and DST method and determining the feasibility of using these methods in our country settings. Sensitivity and specificity of the rapid methods were calculated to determine the efficacy of the methods and Kappa values were calculated to determine the agreement of them with the gold standard in detection of MDR-TB.

Results: Results of first line DST are available for 1504, 950, 837, 1995 samples from solid media, MGIT, LPA and Xpert respectively. In L-J first line DST, 51 (3.4%) were found to be MDR. In Rifampicin resistance detection, the sensitivity/specificity (%) of MGIT was found to be 75/96 in primary and 86/94 in retreatment cases, for LPA 75/97 (primary) and 91/99 (retreatment), and for Xpert 81/99 (primary) and 86/100 (retreatment) respectively. The Kappa values for detection of MDR in primary/retreatment cases with respect to L-J DST were 0.62/0.83 for MGIT, for LPA 0.75/0.95, and 0.75/0.91 for Xpert.

Conclusions: Both the molecular methods, LPA and Xpert showed good agreement with the gold standard in MDR-TB detection in both primary and retreatment cases with little difference between them. Xpert can be used as a good screening tool to detect MDR-TB early. MGIT needs further evaluation in our

settings considering high contamination rates, resource requirements, and relatively poor agreement with gold standard.

PD-1112-29 Accuracy of line probe assays for resistance to rifampicin and isoniazid and detection of *Mycobacterium tuberculosis*: a systematic review and meta-analysis

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Background: Only 25% of multidrug-resistant (MDR) TB cases are currently diagnosed. The development and evaluation of rapid molecular TB diagnostic tests are research and implementation priorities. This systematic review evaluated the diagnostic accuracy of molecular line probe assays (LPA) for rifampicin (RIF) and isoniazid (INH) resistance and the detection of *Mycobacterium tuberculosis*.

Methods: The following databases (PubMed, EMBASE, BIOSIS, Web of Science, LILACS, Cochrane) were searched. Cross-sectional and case-control studies were included. Patients being evaluated for pulmonary TB or MDR-TB were included. Three LPAs were assessed: Hain Genotype MTBDRplus V1, Hain Genotype MTBDRplus and Nipro NTM+MDR-TB detection kit 2. Study quality was assessed using QUADAS-2. Bivariate random-effects meta-analyses were performed for LPA testing on sputum specimens (direct testing) or culture isolates (indirect testing). Results for RIF and INH resistance were compared to phenotypic and composite (incorporating sequencing) reference standards. Results for *M. tuberculosis* detection were compared to culture.

Results: We included 74 unique studies giving 94 datasets. 74 (79%) datasets evaluated patients from low- or middle-income countries. Overall we considered most studies to be at low or unclear risk of bias and applicability concerns were low. Pooled sensitivity and specificity (95%CI) were 96.7% (95.6–97.5) and 98.8% (98.2–99.2) for RIF resistance (91 datasets, 21 225 samples) and 90.2% (88.2–91.9) and 99.2% (98.7–99.5) for INH resistance (87 datasets, 20 954 samples) using data for all three LPAs. Sensitivity and specificity were similar for direct and indirect testing for RIF and INH resistance. Using a composite reference standard, specificity increased to 99.5% (98.6–99.8) for RIF resistance and 99.9% (99.6–100.0) for INH resistance. For *M. tuberculosis* detection (six datasets, 3451 samples), pooled sensitivity was 94% (89.4–99.4) for smear-positive

specimens and 44% (20.2–71.7) for smear-negative specimens.

Conclusions: In patients with pulmonary TB, LPAs have high sensitivity and specificity for RIF resistance. High specificity and good sensitivity were demonstrated for INH resistance. Diagnostic accuracy was similar for direct and indirect testing, compared to phenotypic and composite reference standards. Accuracy for *M. tuberculosis* detection on smear-positive specimens was high. LPAs can be used to expand access to the diagnosis of drug resistance.

PD-1113-29 The TB eXiSt assay for improvement the accuracy of diagnosis of cases with drug resistance

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Background: Determination of *M. tuberculosis* susceptibility to antituberculosis drugs plays one of the key roles in laboratory diagnosis of the disease. For a better management of drug-resistant cases, early and accuracy detection of resistance is extremely important so that effective treatment can be prescribed.

Aim: Implementation of the TB eXiSt assay for improvement the accuracy of diagnosis of TB resistance cases.

Methods: The MGIT 960 system was used for primary isolation of *M. tuberculosis*. 1040 isolated strains were tested for drug susceptibility of INH and RIF using liquid culture method and MTBDRplus ver.2 (Hain Lifescience, Nehren, Germany). The INH resistance strains, found by both methods, but only with inhA mutations, that were interpreted as 'low resistance', were selected for future testing. The MGIT 960 system with the EpiCenter TB eXiST assay was performed for 32 *M. tuberculosis* isolates with low resistance to INH. The high concentration of drugs (INH) was used for DST: 1.0 µg/ml, 5.0 µg/ml and 10.0 µg/ml.

Results: The DST assay have demonstrated: 53.1% ($n=552$) of strains were susceptibility and 41.4% ($n=431$) were resistance to INH by both methods, and in 3.5% ($n=36$) cases were false resistance and 1.5% ($n=16$) false susceptibility. In 0.5% ($n=5$) cases results from LPA were interpreted as 'indeterminate'. From 32 strains with 'low resistance', tested on high concentration of INH, in 15.6% ($n=5$) cases have demonstrated the susceptibility at concentration of 5.0 and 10.0 µg/ml and 6.3% ($n=3$) at 1.0 µg/ml.

Conclusions: The MGIT 960 system with the TB eXiST assay, with implementation of high doses of drugs, could be used for improved the accuracy of MDRTB cases. The correlation of results from

quantitative DST with clinical outcomes, should be helpful for the correction of the treatment regimens and to explain the issue of phenotypic drug resistance levels and treatment failure.

Table DST results on MGIT 960 and MTBDR

MGIT960	Susceptibility	MTBDR _{plus} Resistance	Indeterminate
Susceptibility	552	16	2
Resistance	36	431	3

PD-1114-29 The role of TB-LAMP and Xpert® MTB/RIF assay for the diagnosis of smear-negative pulmonary TB

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Background: Smear negative TB remains a diagnostic challenge in resource-constrained settings. The diagnosis mainly relies on sputum smear examination, but approximately 42% of pulmonary cases are smear-negative. In the absence of sensitive diagnostic method clinician often make the diagnosis of smear-negative pulmonary TB with information obtained through the clinical history, physical examination and chest X-ray. This information is not specific which leads to over or under treatment. Thus, sensitive diagnostic methods have a considerable contribution to decide the appropriate treatment.

Methods: The study was conducted from December, 2014 to June, 2015. All TB presumptive referred to St. Peter TB specialized hospital were enrolled to the study according to the national recruitment criteria. Socio-demographics data, TB symptoms, chest X-ray findings and final decision for anti-TB treatment was collected for each TB presumptive. Spot-Morning-spot sputum was collected for direct ZN examination. The morning sputum was used for culture (LJ and MGIT), TB-LAMP, Xpert MTB/RIF assay and fluorescent microscopy examination.

Results: This study enrolls 459 smear negative presumptive TB patients. Of which 57% (252/442) were Females and median age 40 IQR (28-55) years. The prevalence of HIV among the study participants were 30%. The overall culture positivity rate was 6.8% (30/439), of which 6.6% (26/391) was by MGIT and 5.3% (23/436) was by LJ method. Direct and concentrated fluorescent microscopy adds in 0.9% and 1.3% for smear negative suspects compared to direct ZN. The overall sensitivity and specificity of TB-LAMP was 61.5% (16/26) and 96.6% respectively. The overall sensitivity and specificity Xpert was 70.8% (17/24) and 97.2% respectively.

Conclusions: TB-LAMP and Xpert assay can provide confirmatory result for at least two third of TB cases.

PD-1115-29 Resistance to first-line anti-tuberculosis drugs in Southern Mozambique: results from a population-based drug resistance survey

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Background: Multidrug-resistant tuberculosis (MDR-TB) is a major public health concern in TB control. The last national drug resistance survey in Mozambique was conducted in 2007-2008. No population data on pyrazinamide (PZA) resistance prevalence has been reported in the country. The aim of the study was to determine the prevalence of different TB drug resistance patterns and to describe associated factors to MDR-TB in a rural area of Southern Mozambique.

Methods: Prospective observational study from August 2013 to August 2014 at Manhiça District Hospital (HDM) and Peripheral Health Care Centres whose reference TB centre is the MHC. It covers an estimated population of 110 000. All pulmonary TB presumptive cases providing sputum samples were tested for Xpert MTB/RIF. Those positive were further evaluated for first-line drug susceptibility testing (DST) through liquid culture (MGIT). Prevalence of resistance to different drug combinations was determined as well associations with different risk factors including previous anti-TB treatment, age, gender, HIV status, past imprisonment, alcohol, tobacco and worked abroad.

Results: DTS results were available for 278 patients. Of those, 166 (60,6%) were male and the median age was 33.5 (ICR 26.9–43.8). 39 (14.0%) patients were previously treated. Resistance to at least one first line drug was observed in 46 out of 278 isolates (16.6%: 95%CI 12.6–21.4). Prevalence of drug resistance to five anti-TB drugs tested was: 4.7% for STM, 10.4% for INH, 6.8% RIF, 4.7% EMB and 3.2% for PZA. MDR-TB prevalence was 5.8 % (16/278, 95%CI 3.5–9.2), 4,2% for new cases (95%CI 2.3–7.6) and 15.4% (95%CI 7.0–30.6) for retreatment cases. MDR pattern was more likely among patients who had been previously treated, compared to new cases (aOR = 4.3, 95%CI 1.3–14.1, $P=0.016$). Other risk factors did not have significant association with the MDR pattern.

Conclusions: Results from this survey were similar to those found in a previous national drug resistance survey (although estimates were slightly higher). Retreatment cases showed higher prevalence of almost every resistance (including MDR). Resistance

patterns need to be periodically monitored due to the adverse consequences for patients and health systems.

PD-1116-29 National Anti-Tuberculosis Drug Resistance Survey in the Kingdom of Lesotho, 2013-2014

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Background: Drug-resistant tuberculosis (TB) threatens global TB control. The World Health Organization advises monitoring for drug resistance with ongoing surveillance or periodic surveys. A national anti-tuberculosis drug resistance survey was conducted in Lesotho to estimate the prevalence of multidrug resistant TB (MDR-TB) among smear-positive TB cases.

Methods: During August 2013 - July 2014 all persons with presumptive TB were screened at all existing 18 microscopy centers across the country. All sputum smear-positive individuals were eligible for enrolment. Demographic and TB treatment history information were collected from eligible individuals; HIV status was collected from treatment registers. Two additional sputum samples were tested for genetic mutations that confirm the presence of *M. tuberculosis* and confer drug resistance using GenoType MTBDR^{plus}®. We used multiple imputation model to impute randomly missing drug-resistance results and estimate prevalence of MDR-TB. Multivariate logistic regression was used to calculate adjusted odds ratios (aOR) and 95% confidence intervals (95%CI) of factors associated with MDR-TB.

Results: Among 2528 eligible sputum smear-positive persons, 2044 (81%) were enrolled in the study. Among these, 1861 (73%) were *M. tuberculosis* positive, 55 (2.7%) were *M. tuberculosis* negative, and 128 (6.3%) were not tested or did not have valid laboratory results. Among TB cases, 1569 (84%) were new and 292 (16%) were previously treated; 1036 (56%) were HIV positive. In total, 70 patients had MDR-TB; the majority (66%) were male and 64% were HIV positive. After imputation of missing results for 128 cases, the proportion of cases with MDR-TB was 3.8% (95%CI 2.9-4.6), including 3.2% (95%CI 2.3-4.1) among new TB cases and 6.9% (95%CI 3.9-9.8) among previously treated cases. After controlling for HIV status, previous history of tuberculosis treatment (aOR=1.9, 95%CI 1.1-3.4) and age group 45-54 years old (aOR=3.0, 95%CI 1.5-6.2) were significantly associated with MDR-TB.

Conclusions: Prevalence of MDR-TB among new TB

cases in Lesotho is concerning and consistent with the results of a previous survey conducted in 2008–2009 and with the prevalence of MDR-TB in surrounding countries. Lesotho should consider the feasibility of routine anti-TB drug resistance surveillance on initial diagnostic specimens to improve timely and accurate MDR-TB diagnosis.

PD-1117-29 Results of the national anti-tuberculosis drug resistance survey in Senegal: an innovative approach using rapid molecular technologies

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Background: In countries without capacity for routine drug susceptibility testing of all tuberculosis (TB) patients, WHO recommends periodic surveys. The previous national survey conducted in 2006 in Senegal found 2.1% (95%CI 0.7–4.9%) multidrug-resistant TB (MDR-TB) in new patients and 17.0% (95%CI 7.0–31.0%) in previously treated patients. The survey completed in Senegal in 2014 is the first national anti-TB drug resistance survey globally to rely exclusively on rapid molecular technologies to screen patients for drug resistance.

Methods: The survey was conducted in 30 clusters selected using a probability-proportional-to-size approach. All new and previously treated TB patients meeting the inclusion criteria were enrolled. Sputum samples were preserved in 1% CPC and tested by the Xpert® MTB/RIF assay at peripheral or central testing sites. Culture on Löwenstein-Jensen media was performed only for sputum samples with resistance to rifampicin or any samples from previously treated patients. Drug susceptibility testing of culture isolates was performed by conventional phenotypic testing and line probe assay (Hain GenoType MTBDR_{plus}). External quality assurance was performed by the Institute of Tropical Medicine in Belgium.

Results: The survey enrolled 812 new and 95 previously treated patients, of which 70% were male. The median age was 30 years (range: 6–87 years). The proportion of new patients with MDR-TB was 0.5% (95%CI 0.1–1%) and 17.9% (95%CI 9.3–23.2%) among previously treated cases. A valid result for rifampicin status was available for all eligible patients. A result for isoniazid was available for all patients with rifampicin resistance.

Conclusions: The burden of MDR-TB remains low in

Senegal, particularly among new TB patients. Levels of resistance are significantly higher among previously treated patients and routine testing for rifampicin resistance should be prioritized among this group. The innovative design of this survey, based on screening by Xpert, greatly reduced logistic challenges for sample transport and testing. Laboratory testing results were consequently available for all survey participants, minimizing the risk of bias due to missing data. This simplified approach can serve as a model for other countries planning surveys to estimate the burden of anti-TB drug resistance.

PD-1118-29 Study on pyrazinamide resistance of *M. tuberculosis* in Viet Nam: making comparisons between two national surveys

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Background: Pyrazinamide (PZA) is one of the important anti-TB drugs used in tuberculosis and multidrug-resistant treatment. Viet Nam lacks PZA resistance information for *M. tuberculosis* resistance because the DST method is not suitable for PZA. Study in PZA resistance by appropriate method applied on the strains collection of two Drug Resistant National Surveys (DRS) and finding the trend of PZA resistance are the key objectives aims to provide useful information for the National TB program

Methods: Testing PZA resistance by detection method of enzyme activity (Waye method) used on the collections of *M. tuberculosis* strains following 3rd and 4th nationwide drug resistance surveys (2005 and 2011). Compared the results between the new TB, previously treated-TB, MDR patients and finding the trend of PZA resistance of two strain collections

Results: Characteristic of PZA-resistant strains: 45.5% resistant PZA combining 4 other first-line TB drug: RMP, INH, SM, EMB; 70% PZA-resistant strains also being multidrug-resistant ones (60% among new TB and 100% in the previously treated group) (result in 2011)

Conclusions: In Viet Nam, PZA resistance rate is low (0.5 to 2.2%). However, it rapidly increased in 6 years (compared 2011 to 2005), increased 4 times for new TB and 3 times for previously treated patients. Especially, it ups to 14 times to MDR patients (18.5%). The majority of PZA-resistant strains are multidrug-resistant. It is necessary to continue monitoring PZA resistance in Viet Nam and have further studies for epidemiological PZA resistance finding.

Table A) PZA resistance among new and retreatment TB patients

Category	2005 DRS		2011 DRS	
	Total strains	% PZA resistance	Total strains	% PZA resistance
New patients	1593	0.4	1373	1.8
Previously treated	182	1.7	127	5.9
Combined	1775	0.5	1400	2.2

B) PZA resistance among MDR patients

Category	2005 DRS		2011 DRS	
	Total strains	% PZA resistance	Total strains	% PZA resistance
MDR-TB	77	1.3	124	18.5
Others	1698	0.5	1276	0.7

PD-1119-29 Reduction in treatment delay of MDR-TB cases as a result of Xpert® MTB/RIF implementation in Moldova

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Background: Since 2012, the Republic of Moldova, a high burden MDR-TB country received external financial support for programmatic implementation of Xpert MTB/RIF rapid test for TB diagnosis. One of the expected benefits from this intervention was to reduce time from TB diagnosis to MDR-TB confirmation for prompt MDR-TB treatment initiation. The current study aimed to assess the duration of treatment delay in MDR-TB patients before and after implementation of Xpert in Moldova.

Methods: The authors assessed the treatment delay in all MDR-TB cases registered in the national electronic TB database (SIME-TB) during 2011-2015. Treatment delay was defined as the time between TB diagnosis (before resistance pattern confirmation) and initiation of MDR-TB treatment. A yearly comparison of treatment delay before and after implementation of Xpert was performed. The correlation between treatment delay and number of the performed Xpert tests was calculated.

Results: 4001 MDR-TB cases registered in SIME-TB were included in the final analysis. The median treatment delay in 2011, the year prior Xpert implementation, was 42 [13-79] days. In the first year of Xpert introduction in clinical practice (2012), no significant reduction in the treatment delay was achieved 32 [10-65] days ($P=0.08$). However, a progressive reduction in treatment delay has been registered during next three years: in 2013 treatment delay was 20 [5-53] days ($P<0.001$), in 2014 - 8 [2-28] days ($P<0.001$) and in 2015 - 7 [2-18] days ($P=0.02$). A strong correlation between the number of

the performed Xpert tests and reduction of treatment delay ($r=0.92$; $P=0.002$) was registered.

Conclusions: Implementation of Xpert rapid test led to a significant reduction of treatment delay in MDR-TB cases in the Republic of Moldova, thereby leading to a better clinical management of these cases.

PD-1120-29 Implementation of a molecular diagnostics program to improve TB case detection in Malawi

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Background and challenges to implementation: Project HOPE is working with the Government of Malawi (GoM) to increase case detection in 12 districts in Malawi (population 6 000 000). Case detection has been low in Malawi due to use of microscopy as the main diagnostic method and a passive approach where patients presumed to have the infection report to health facilities on their own time, often very late. Until 2011, health facilities providing novel TB diagnostic facilities were not easy to access resulting in missed or late accurate diagnosis leading to high mortality among TB patients.

Intervention or response: In 2011, Project HOPE and GoM introduced GeneXpert machines in high volume health facilities and maintained sputum quality through the timely provision of transport from peripheral collection points to GeneXpert sites and cold chain support. Laboratory technicians were trained, and algorithm was developed on its use, and health care workers were orientated on FAST approach in identifying presumptive TB cases.

Results and lessons learnt: From 2014 - 2015, 24 271 and 5179 tests were performed in TB-REACH primary and secondary support districts respectively, representing 21% increase in tests. During this period, 3,601 (12.2%) MTB+ cases were identified from intervention districts. The increase in number of sputum samples tested is attributed to continuous support of transportation of sputum from peripheral health facilities to GeneXpert sites. The project provided one motorcycle and fuel to each of the supported districts. Refrigerators were also provided to maintain cold-chain system.

Conclusions and key recommendations: Use of GeneXpert machines has increased the detection of bacteriologically confirmed TB cases in TB-REACH intervention districts of Malawi. Districts need sputum transportation and cold chain maintenance support to effectively implement Xpert testing for presumptive cases from peripheral areas.

52. Key populations: all in

PD-1121-29 Identifying challenges in TB treatment adherence and cross-border referral among migrant workers in the mining sector in Southern Africa

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Background: The incidence of TB in South African (SA) mines is estimated at 2500-3000/100 000 people - more than 3 times higher than the general SA population and ten times the level of World Health Organization's emergency threshold of 230/100 000. Miners who are diagnosed with TB are at risk for TB treatment non-adherence and lost-to-follow-up when returning to labour-sending areas. We conducted an elicitation study to understand barriers to and potential promoters of TB treatment adherence and cross-border referrals as part of a trial assessing the effectiveness of multi-level intervention packages to improve adherence.

Methods: The elicitation study was conducted at two large mines in SA which employ large numbers of migrant miners from Mozambique, Swaziland and Lesotho. Data was collected using four methods: a) a scoping review of the literature, b) stakeholder consultation which involved focus group discussions (FGD) and an online survey with key stakeholders from, c) FGDs with mineworkers who had TB and had travelled home while on treatment, and d) FGDs and a comprehensive survey with mineworkers on current TB treatment. Qualitative data was analysed using content analysis; survey data was summarised using descriptive statistics.

Results: There were many areas of convergence across the different data sources. Individual-level barriers to adherence to treatment and care included belief in superiority of home country TB regimens, quality of life whilst on treatment, traditional beliefs regarding illness, lack of information about TB treatment, stigma, and alcohol use. Some structural/systemic barriers included disempowered/top-down care, lack of access to services and poor infrastructure in home countries, SA migration laws, poor referral chains, lack of family support and staff attitudes and availability. Themes that emerged around possible promoters of adherence and referral included the promotion of harmonised treatment, patient psychosocial support, more thorough health education for patients and staff, and a well-coordinated and closely monitored cross-border referral system.

Conclusions: The findings from this study present an opportunity for developing multi-pronged, evidence-

based intervention packages to address the problem of TB treatment non-adherence and ineffective cross-border referral mechanisms. However these interventions must be context-sensitive, acceptable and sustainable to ensure long-lasting impact and scaling-up.

PD-1122-29 Finding the missing cases: active TB case finding in communities in two mining districts in Zimbabwe

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Background: Mining community has long been associated with a high prevalence of various lung diseases, including tuberculosis (TB). Contributing factors include a high prevalence of silicosis resulting from prolonged exposure to silica dust, high rates of HIV transmission and confined, humid, poorly ventilated working and living conditions and limited access to health services. The USAID TBCARE II project, managed by University Research Co., LLC (URC), supported a pilot test of the feasibility of active TB case finding in two districts that have significant small-scale and artisanal mining activities. **Methods:** Two districts in two provinces with high mining activities, especially informal mining, were purposefully selected, and sites within the districts were selected for the mass screening effort. A multi-disciplinary awareness and demand creation team visited the selected sites a week before screening commenced. The screening team used a truck equipped with a digital X-ray machine for chest radiograph, sputum collection and HIV testing materials. Two teams conducted TB mass screening between October and December 2015 at 16 sites in the two districts.

Results: In total, 7508 clients were screened, of whom 6148 (82%) had completed questionnaires. Of these, 2686 (44%) were male, 3385 (55%) were female and 1% did not indicate gender; 726 (12%) were formally employed and 1367 (22%) were artisanal miners. Of the latter, 394 (29%) were female. During the active case finding exercise, 2861 clients were tested for HIV and 359 (13%) were positive. A total of 129 TB cases (1,718 case per 100 000 population) were newly diagnosed and enrolled on treatment.

Conclusions: The prevalence of TB in these per-mining communities is more than four times higher than the national prevalence of 344 cases/100 000 population found by the 2014 national TB prevalence survey. Active case finding was feasible and resulted in additional TB cases being put on treatment.

PD-1123-29 Will repeat household visits for active case finding in key affected populations yield results?

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Background and challenges to implementation: India accounts for 2.1 Million (one fifth) of the 9.6 million cases which occurred in 2014. Out of 3.6 million unreported or missing cases worldwide around one million are thought to be from India. These unreported or missing cases are mainly from the Key Affected Population (KAP) such as urban slums and or accessing the private health sector.

Intervention or response: Population Services International (PSI) is conducting Active Case Finding among the urban slum populations in two municipal corporation areas Kolhapur and Sangli in Maharashtra, India, under Project Axshya. The trained community volunteers, from the same community conduct household visits among Key Affected Populations (KAP) in urban slums to identify TB symptomatic and link them to Designated Microscopic Centres (DMC) for TB diagnosis. We conducted Active Case Finding in urban slum of Kolhapur and Sangli Municipal Corporation covering more than 17,000 households. First household visits were done during Oct'13 to June'14 and second household visits were done during July'14 to Mar'15.

Results and lessons learnt: We compared the results of first contact and second contact to the same households, the analysis showed that during the first contact total 503 TB symptomatic were identified and referred, out of these 16 were diagnosed with TB. During the second contact in the same area within a span of 9 months, 326 TB symptomatic were identified and referred for sputum testing, 17 of them tested positive for TB.

Conclusions and key recommendations: Single contact of households may not be sufficient to identify TB symptomatic from the communities as part of Active Case Finding. Repeat visits to the same KAP population yields good results. Detailed study is recommended to assess the frequency of visits for Active Case Finding among the Key affected population.

PD-1124-29 Patient costs of accessing tuberculosis diagnosis among high-risk communities in Kampala, Uganda

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Background: Direct and indirect patient costs have been identified by several studies as barriers to TB diagnosis and care, especially due to the catastrophic expenditure impact on households. Several strategies have been proposed to improve TB case identification but little is known of the costs incurred by the patient to the point of TB diagnosis. Kampala is the highest TB burden district in Uganda where one in every five TB cases in the country is detected. We carried out a study to determine the costs of accessing diagnosis for drug susceptible and multi-drug resistance TB in Kampala.

Methods: Patient and household direct and indirect costs were assessed from a survey of 100 newly diagnosed pulmonary TB and MDR-TB patients in the intensive phase of treatment, systematically sampled from six main health facilities (public and Private-not-for-profit) which notify the largest number of TB patients in Kampala. Adult patients coming from TB high burden communities were considered and those that were HIV positive. A standardized WHO costing tool (21 indicators that suite the study setting were adopted for use) was used for data collection. The tool included parameters on monthly income for the patient/caregiver, time lost off work (for the patient or caregiver for the period prior to TB diagnosis), cost of transportation, costs of investigations for TB, among others.

Results: Pulmonary TB patients incurred US\$ 21 (or 13 days' income) and lost 10 days on average away from work while seeking TB diagnosis. For MDR-TB patients, the total costs to diagnosis amounted to US\$ 100 (or 54 days' income) which approximated to 129% of the average total monthly income.

Conclusions: The indirect costs incurred by TB patients, especially for MDR-TB and their households are unacceptably high even where TB diagnostic services are provided free of charge. Thus, there is need to urgently address this issue so as to overcome the prohibitive catastrophic healthcare expenditures by the poor individuals. There is also need to come up with cost effective strategies to provide TB services for the poorer high risk communities.

PD-1125-29 Poverty predisposes patients to intermittent adherence to TB treatment

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Background: Poverty is an important barrier to TB treatment adherence. Intermittent adherence is frequent and a major determinant of adverse treatment outcomes and TB recurrence. In order to understand factors underlying intermittent treatment adherence, we aimed to characterize the association of clinical and socioeconomic factors with a new operational definition of intermittent adherence.

Methods: We performed a prospective cohort study January 2003-January 2013 in 16 peri-urban shanty-towns in Ventanilla, Peru. Patients with TB commencing treatment with standard first-line anti-TB therapy from the Peruvian National TB Program were invited to participate. Patients received at least all doses of intensive phase treatment. Intermittent adherence was defined as missing ≥ 4 doses during the intensive phase or missing ≥ 5 doses during the maintenance phase. These missed doses were postponed, so prolonged time to complete therapy. We used principal component analysis to generate a composite poverty index incorporating socioeconomic factors including education, access to services, assets and housing quality.

Results: Of 2217 recruited patients, a defined adherence condition was available for 2021. Of these, 954 (47%) had intermittent adherence. These patients were more likely to have poorer poverty score (RR=1.2, $P=0.02$) and misuse drugs and/or alcohol (RR=1.3, $P=0.003$).

Conclusions: Intermittent adherence occurred more often in marginalized patient subgroups such as poorer patients and substance abusers. In a cluster-randomised evaluation, we will investigate whether socioeconomic support provided to impoverished TB affected households may incentivize and enable access to TB care and thus improve adherence in these groups.

Table Factors associated with intermittent adherence

Characteristic	Non-intermittent adherence n/N (%, 95%CI)	Intermittent adherence n/N (%, 95%CI)	RR (95%CI)	P value
Poverty score (lowest tercile)	309/1027 (30, 27–33)	341/899 (38, 35–41)	1.2 (1.1–1.3)	<0.001
Drug or/and alcohol abuse	142/1016 (16, 13–18)	183/892 (23, 20–26)	1.3 (1.1–1.4)	<0.001

PD-1126-29 Institutionalizing systematic screening for early TB case finding among PLHIV: progress and challenges in Nepal's Tuberculosis Program

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Background and challenges: Early TB diagnosis requires a systematic screening at right time in identified people who are at risk of developing Tuberculosis (TB). Therefore, World Health Organisation (WHO) suggests to conduct screening in the right way and targeting the right people for early TB case finding. However, Nepal's TB Program (NTP) with TBHIV co-infection strategy is still struggling in both find early TB and reducing TB associated death among high risk groups such as PLHIV. The UNOPS funded TB REACH project of Naya Goreto (NG) has implemented intensified TB case finding as a part of tackling TB in underserved key populations especially People Living with HIV (PLHIV).

Intervention: Naya Goreto conducted an intensified TB case finding among PLHIV and other vulnerable groups in 10 districts of Nepal in 18 months. The project was able to reach at 8110 (aged 15–64) key populations for early TB screening and diagnosis. Ex-PLHIV-TB co-infected patients were extensively mobilized as project volunteers for both active TB case finding and contact tracing with a simple but systematic TB screening form and IEC/BCC materials.

Results and lesson learnt: Despite a massive earthquake, project succeed to reach at 8110 for early TB screening and found 287 TB cases; and able to systematize TB screening as a part of routine health check-up especially in CD4 counting and ART enrollment process. The institutionalization of regular TB screening practice among PLHIV and other vulnerable groups is the key outcomes of this project. The proliferation of TB related health seeking behavior among them after project broke the reluctance of key population to engage in TBHIV program of Nepal.

Conclusions and key recommendation: In short period, this project was successful to institutionalize systematic TB screening among key populations as a part of their health care. Desirable behavior change in hard to reach significantly contributed to early diagnosis of TB, timely access to TB treatment, and reduction in TB associated death among key populations. NTP should maintained and placed this newly institutionalized early screening and diagnosis system at the center of its program primarily in TBHIV co-infection strategy for achieving its targeted goals.

PD-1127-29 Hospitalizations due to tuberculosis and social inequality: a spatial analysis in an endemic city in São Paulo, Brazil, 2006-2012

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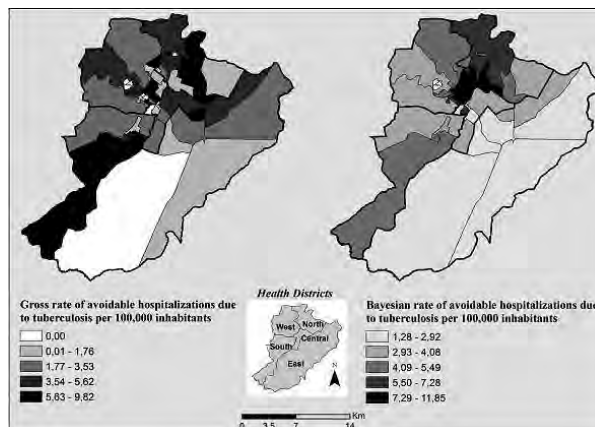
Background: Hospitalization by tuberculosis (TB) is an indicator of lack of access to Primary Health Care services. Areas with severe social problems tend to have PHC services with lower quality and problem solving ability, not contributing to the elimination of TB in the community. Thus, the goal was to identify whether hospitalizations by TB are related with areas of social inequality.

Methods: Ecological study that considered the hospitalizations by TB registered between 2006 and 2012 in the Hospitalization System of the Unified Health System. In addition, the variables literacy of Family heads, number of people per residence and per capita income of the residence were considered, obtained through the 2010 Demographic Census of the Brazilian Institute of Geography and Statistics. Principal Components Analysis (PCA) was performed in the software Statisticato construct the indicators. Geocoding was developed in Terraview 4.2.2. The hospitalization rate by TB was calculated with smoothing using the local empirical Bayesian method. Territories under the responsibility of a PH service were defined as the geographical unit. Multiple linear regression, spatial dependency test and spatial regression were used to analyze the relation between the hospitalization rates due to TB and the indicators of social inequality in the software R.

Results: The rates ranged between 1.28 and 11.85 hospitalizations per 100 000 inhabitants/year. In the PCA, three indicators were constructed, with a variance of 46.21%; 18.76% and 14.61%, respectively. In the multiple linear regression, the income indicator was statistically significant ($P=0.015$), with a negative estimate (-0.24), an adjusted R^2 of 28.36% and spatial dependence (Moran $I=0.48$, $P<0.0001$). The best model to treat the spatial dependence was the Spatial Lag, which evidenced a negative correlation with income. Hence, for each unit increase in the income, the hospitalization rates by TB would drop by 0.24 cases for every 100 000 inhabitants.

Conclusions: The areas with better income distribution show lower TB hospitalization rates, evidencing that hospitalization due to the disease is a socially determined event, underlining the importance of social protection through universal systems for the advance of its elimination, according to the target set for 2050.

Figure Map of hospitalization rates for TB



PD-1128-29 TB and poverty: do we really care?

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Background: India is one of the few developing countries with a steady economic growth. However, it continues to have the highest burden of poverty-related diseases including Tuberculosis (TB). Every fifth TB case is from India. Throughout the world poor and disadvantaged social groups are affected disproportionately by TB. The risk factors for TB like poor hygiene, over-crowding, poor sanitation, malnutrition and others are encompassed in poverty. The economic burden caused by TB continues to push the families into poverty, creating a vicious cycle.

Methodology: A community based knowledge, attitude and practice (KAP) about TB among general population (GP) and TB patients conducted in 2013 provides profile of TB patients and their counter parts from GP across 45 districts in India. The survey instrument captured the KAP along with demographic and economic information. A Standard of Living Index (SLI) was calculated as per the National Family Health Survey guidelines. Numerical scores were given based on the presence or absence of the household amenities and added to derive a composite score. A score of 0-17, 18-24 and 25-60 indicates low, medium and high SLI respectively.

Results: A total of 7225 people from GP and 644 TB patients were interviewed from both rural and urban settlements. Majority of the GP fall under high SLI group (42%) followed by medium (36%) and low (22%). However, among TB patients majority are from the medium SLI (41%), followed by low (32%) and high (27%). Majority of TB patients (54%) earn < Rs.4000 (~\$60) per month whereas majority of the GP (50%) earn > Rs.4000. Most TB patients (67%) use wood as cooking fuel as compared to GP (60%)

exposing them to indoor air pollution. It was also observed that more TB patients were illiterate (44%) as compared to GP (29%).

Conclusions: Most of the TB patients are still affected by poverty and there is disparity amongst the TB patients and GP in terms of economic status. Exclusive policies and economic reforms to uplift TB patients and their families are required to break this vicious cycle. Strong and sustained efforts to alleviate the poor may hasten TB elimination.

PD-1129-29 Systematic facility- and community-based screening for TB in Phnom Penh, Cambodia

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Background and challenges to implementation: Although Cambodia has made significant progress in reducing its TB burden, the 2011 prevalence survey showed many people with TB are still missed by existing health services. The Sihanouk Hospital Center of HOPE (SHCH) set out to address this issue by implementing an active case finding (ACF) program in two key populations: patients and their attendants in two hospital waiting areas and people living in urban slums, and poor communities in Phnom Penh and Kandal.

Intervention or response: All people were first verbally screened for TB symptoms. In the urban slums, two mobile chest x-ray (CXR) vans were deployed, while the hospitals had stationary x-ray systems. All symptomatic people and people aged 50 or above received a chest X ray (CXR), sputum smear microscopy, or/and an Xpert MTB/RIF test. People with an abnormal CXR whose first smear was negative, then had their second sputum sample tested with the Xpert assay. For symptomatic people whose CXR was normal, two smear tests were performed.

Results and lessons learnt: During the intervention, 1,174 people with symptoms were identified in the two hospitals, compared with 8381 people in the community. This screening and diagnostic approach identified 62 (5%, number-needed-to-screen: NNS 19) people with bacteriologically-confirmed TB in the two hospital, compared with 169 (2%, NNS 50) in the community. A similar difference in yield was observed among all forms TB detection (115 [10%, NNS 10] in hospitals vs 385 [5%, NNS 22] in the community). Bacteriologically-confirmed TB comprised 54% of people with TB in the two hospitals compared with 44% of people with TB in the community.

Conclusions and key recommendations: Screening for

active TB in hospitals had a yield rate double that of community-based ACF. However, in terms of absolute numbers, the community strategy identified more people with TB. In order to meet the End TB Strategy goals, more intense screening of people visiting existing health facilities is needed. In addition, community-based ACF is a vital tool to identify people with TB who are missed by health services.

PD-1130-29 Innovative contact-tracing strategy within a 50 m radius of index tuberculosis cases using Xpert® MTB/RIF in Pakistan: did it increase case detection?

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Background: Currently, only 62% of incident TB cases are reported to the national programme in Pakistan. Several innovative interventions are being recommended to detect the remaining 'missed' cases. One such intervention involved expanding contact tracing to the community (households within 50 metres of an index case) using Xpert MTB/RIF.

Objectives: To determine the impact of contact investigation beyond household on TB case detection in Pakistan.

Methods: This was a before and after intervention study involving retrospective record review. July 2011-June 2013 and July 2013-June 2015 was the pre-intervention and intervention period respectively. Four districts with a high concentration of slums were selected as intervention areas which included Lahore, Rawalpindi, Faisalabad and Islamabad. While passive case finding and household contact investigation was routinely done in all districts, contact investigation beyond household was done in intervention districts: all people staying within a radius of 50 metres (using GIS) from the household of smear positive TB case were screened for tuberculosis and those with presumptive TB were investigated using smear microscopy and as a part of intervention, first time in Pakistan, Xpert test was applied for smear negatives. All the diagnosed TB cases were linked to TB treatment and care.

Results: A total of 783 043 contacts were screened for tuberculosis: 23 720 (3%) presumptive TB cases were identified of whom 4710 (23%) all forms and 4084 (20%) bacteriologically confirmed TB cases were detected. The contribution of MTB/Xpert to bacteriologically confirmed TB cases was 14%. The screening yield for child TB cases among investigated presumptive child TB cases was 5.1%. The overall yield of all forms TB cases among investigated was 23% among household and 20% in close community.

The intervention contributed an increase of case detection of bacteriologically confirmed tuberculosis by 6.8% and all forms TB cases by 7.9%. Number needed (NNS) to screen to detect one confirmed TB (all forms) among total contacts screened was 77 among household contacts and 195 among close community contacts.

Conclusions: Community contact investigation beyond household not only detected additional TB cases but also increased TB case detection. However, further long term assessments and cost-effectiveness studies are required before national scale-up.

53. Cost: socio-economic impact on TB

PD-1131-29 High return in TB diagnosis and treatment with low investment in tribal and extremist areas of Jharkhand, India

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Background: The second principle of WHO END TB Strategy emphasizes on strong coalition with civil society and advocates for impudent policies/supportive system to eliminate TB. The National Strategic Plan of India accentuates in bridging the gap between patient and provider. Jharkhand, mining hub of India with 26% tribal population and presence of left wing extremism in 60% areas has been implementing RNTCP since 2000. Civil Society and Corporate are two major players in diagnosis and treatment along with public sector. This paper tries to highlight the growing role of Non-State actors in the vision of TB free world.

Intervention or response: 329 microscopy and treatment centres were established to cover 35 million population that include 260 (79%) in tribal/rural areas by 2015. 11 such centres in tribal areas run by CSOs and 19 by Corporates of Public and Private Sectors. 4 centres are supported financially under the programme. The analysis is done on direct contribution of 30 centres being run in 11 (46%) of 24 districts in terms of case notification during 2014.

Results and lessons learnt: 36045 TB cases notified during 2014 that include 22509 smear positive with 14213 (63%) from those 11 districts with 1084 (8%) from CSOs and corporates. This includes 620 by CSOs; 464 by PSUs/Corporate. The paradox is 8% contribution came from 3% population coverage. Sputum positivity rate in CSOs run centres was 13% and 9% in PSUs against 12% of the state.

The 4 centres financially supported under programme, contributed 314 Sm +ve TB cases against the grant of \$9000 i.e. about US\$28.5 per case against nearly US\$50 being spent in the system. Further, 770

Sm +ve TB cases were diagnosed directly by CSOs/PSUs/Corporates with zero cost..

Conclusions: The analysis reveals, return is much higher against investment in tribal and hard to reach areas in terms of TB case diagnosis and treatment. Approach of inclusion of other sectors needs to be widened and there is need of thinking beyond the approach of system controlled to partnership mode. Collaboration pace between public & private is negligible. Decision makers to think for more space for such coalitions.

PD-1132-29 Towards zero TB-affected households facing catastrophic costs: the role of governmental cash transfer programmes

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Background: Financial costs incurred by Tuberculosis (TB) patients have previously been defined as catastrophic when they exceed 20% of an affected households' annual income. The post-2015 END TB strategy endorses social protection policies, including cash transfer programmes, to eliminate all TB patients' catastrophic costs by 2020.

Methods: We used published data in nine selected countries to estimate the potential of governmental cash transfer programmes to mitigate TB patients' catastrophic costs. Countries were eligible if they had a governmental family targeted cash transfer programme, published TB patient average cost data and had a recent household income and expenditure survey. The potential of programmes to mitigate catastrophic costs was calculated as: the percentage point (%pt) difference in average TB patient costs as a percentage of countries' average annual household income in the poorest quintile, before and after addition of the total value of cash transfers expected to be received by beneficiary households over one year. Where cash transfers did not reduce average TB patient costs to below 20% of average annual household income, we calculated the additional value of cash necessary to achieve this. For analysis, all

monetary values were inflated and converted to 2013 international dollars using purchasing power parity conversion factor.

Results: Before addition of cash transfers, average TB patient costs were catastrophic in six out of nine selected countries. Across countries, the potential of cash transfers received over one year to mitigate TB patients' catastrophic costs by adding to average annual household income varied widely (0.3%pt difference to 31%pt difference). After addition of cash transfers, average TB patient costs remained catastrophic in all six of the countries in which they were originally greater than 20% of average annual household income (22% to 78%). In these countries the value of additional cash necessary to mitigate catastrophic costs ranged from \$108 to \$6200.

Conclusions: While governmental cash transfer programmes might reduce the severity of TB patients' catastrophic costs, additional innovations may be needed to confront the challenge of eliminating TB catastrophic costs by 2020.

PD-1133-29 Impact of the new financing and payment model on TB patients' financial burden in China

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Background and challenges to implementation: China is one of the countries with highest tuberculosis (TB) and multi-drug resistant tuberculosis (MDR-TB) burden. Although first-line TB drugs are dispensed free of charge, Chinese patients still have to pay for other medical services out-of-pocket, and bear a large financial burden. In order to improve the accessibility of TB treatment and reduce patients' financial burden, the Gates Foundation, in collaboration with the Chinese government developed a new financing and payment model to improve reimbursement rate and implement case-based payment for TB treatment. Three cities -Zhenjiang, Yichang and Hanzhong representing different stages of economic development in China were selected as study sites.

Intervention or response: Health insurance department and civil affairs bureau improved reimbursement rate to minimally 70% for ordinary TB, and 80% for MDR-TB patients. Standard service packages with fixed payment rates were designed for TB and MDR-TB cases. Patients only need to pay a portion of the actual cost, maximally the payment rate, for services within the package. 832 and 798 patients from 9 counties (3 in each city) were

surveyed respectively at baseline and final evaluation to collect information about their socio-economic status, treatment experience and cost. Patients' medical records and payment information were retrieved from hospitals.

Results and lessons learnt: The out-of-pocket payment per hospital admission decreased from RMB 2218 to RMB 1901. The actual reimbursement rate increased, reaching 63%-71% for ordinary TB inpatient services in all project cities, and 81% for MDR-TB in Zhenjiang. The percentage of patients in debt due to medical expenses decreased from 31% to 20%. Nevertheless, medical services excluded from the packages were often provided to patients. The percentage of patients who incurred catastrophic medical spending remained 70% for TB and 80% for MDR-TB. The total treatment cost modestly increased during intervention period in all project cities.

Conclusions and key recommendations: The new financing and payment model has limited effects in reducing TB patients' financial burden, mainly due to an overall increase of treatment cost. Resources from multiple channels should be mobilized to increase reimbursement rate, and case-based payment should be implemented with more supporting policies.

PD-1134-29 Financial incentives for patients to reduce household catastrophic payments for tuberculosis care in rural Nigeria: implications for the End TB strategy

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Background: The elimination of catastrophic costs that tuberculosis (TB)-affected families face is a target of the End-TB Strategy. This study aimed to evaluate the feasibility and the impact of financial incentives in reducing catastrophic payments for TB care in a high-burden resource-poor setting.

Methods: A pragmatic-controlled implementation design was employed. We prospectively enrolled all TB patients during April to June 2014 in a rural health facility from one district (intervention arm). Patients in the intervention arm received \$15 per month for six months. All patients registered during the same period in two rural health facilities from another district were enrolled as the control arm. Costs and income data were collected at intervals until the end of treatment using a standardized questionnaire. Catastrophic payment is costs >40% of non-food income. We used logistic regression analysis to identify the determinants for catastrophic payments.

Results: A total of 205 patients were surveyed; 121

and 84 in the intervention and control arms, respectively. The patients did not differ according to their demographic or clinical characteristics ($P > 0.05$). The median (IQR) direct cost of care in the intervention arm was \$86.8 (28.0 - 166.2) and \$149.4 (100.9 - 178.8) in the control arm ($P < 0.001$). The overall incidence of catastrophic payments for TB care was 10.7% (13/121) in the intervention and 59.5% (50/84) in the control arm ($P < 0.001$). In the intervention and control arms, catastrophic payments occurred in patients belonging to the lowest two income-quintiles in 17.3% (14/81) and 63.2% (48/76), respectively. Independent determinants for catastrophic payments were; female gender (aOR 6.2), HIV-negative status (aOR 4.5), not receiving financial incentives (aOR 21.0), and lower household income (aOR 1.1).

Conclusions: Financial incentives reduce catastrophic payments for TB care. Providing monetary incentives to patients may add substantial value to TB control. These observations should inform the End-TB strategy.

PD-1135-29 Do households face catastrophic expenditure because of tuberculosis disease in India?

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Background: In India, > 50% of the tuberculosis patients prefer private providers and many undergo treatment irrespective of their income. With prevalence among poor being at 1100 per 100 000 population compared to 201 per 100 000 in total, one always ask this question - Is there a catastrophic expenditure among poor because of tuberculosis?

Methods: We used National Sample Survey Organization (NSSO) data published in 2014 that reported health service utilization and health care related out-of-pocket (OOP) expenditure by income quintiles and by level of care (public or private). The recall period for inpatient hospitalization expenditure was 365 days. Consumption expenditure was collected for a recall period of 1 month. OOP expenditure amounting to more than 10 per cent of annual consumption expenditure was termed as catastrophic.

Results: Overall there were 610 registered out-patient care consultations and 299 as in-patient care (hospitalization) for Tuberculosis. OOP for out-patient care in public is averaged at 1.7\$ and for private is 7.7\$. This is inclusive of direct and indirect cost. The borrowings are significant in public sector utilization of care. Borrowings were more among second quintile at 4.4% leading to 0.2% of households in this quintile to catastrophe. However, 2.2% of households in first quintile faced catastrophic burden

of tuberculosis disease. OOP for in-patient care in private (205\$) was >5 times that of public sector (38\$). Borrowings were highest among second quintile. 53% of first quintile and 44% of fourth quintile faced catastrophic burden as a result of TB disease. In addition fourth and fifth quintile spent nearly 102\$ (13-297) and 291\$ (57-308) for inpatient care respectively.

Conclusions: OOP expenditure for in-patient care leading into catastrophe among households is evident pushing poor to more poorer. Borrowings or sale of assets have been major coping strategies. Evidences suggest need for insurance mechanism to support tuberculosis patients.

Table Out of pocket expenditure for OPD and IPD among quintiles

Table 1 OOP expenditure for OPD and IPD among Quintiles

Quintiles	OPD		IPD	
	(USD)	Catastrophe (%)	(USD)	Catastrophe (%)
First	3.1 (2.5-4.6)	2.2	54 (31-151)	53
Second	7.9 (3.2-18.5)	0.2	74 (25-171)	28
Third	13.8 (5.5-18.8)	0	80 (40-232)	29
Fourth	3.8 (1.0-21.7)	0	102 (13-297)	44
Fifth	1.1 (1.1-3.5)	0	291 (57-308)	26
Overall	3.4 (2.3-13.5)	1.2	82 (25-251)	38

OPD: Outpatient care, IPD: In-patient care

PD-1136-29 Factors associated with borrowing money or selling assets among new tuberculosis patients during their treatment

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Background: Tuberculosis (TB) treatment in Tanzania has been available free of charge to all TB patients for over 25 years. However, not all patients suffering from TB can afford to get treatment without any obstacles, especially financial constraints. We, therefore, determined factors associated with TB patients borrowing money or selling their assets due to the illness.e strategies which will be used to assist TB patients to cope with the costs due to TB illness.

Methods: A cross-sectional study was conducted in one urban and two rural districts in Tanzania among TB patients receiving anti-TB under home-based care. We measured TB patient's direct and/or indirect cost as well as coping costs using WHO guidelines.

Results: Of the 88 home-based TB patients, 58% were borrowing money mainly from neighbours and friends or were selling their assets during TB treatment. In comparing direct and indirect costs against the estimated income to home-based TB patients for the six-month treatment period, TB patients spent more than 75% of their income on

TB illness. Older age, illiteracy and longer time taken to reach the health facility were associated with borrowing money or selling assets to cope with the costs due to TB illness.

Conclusions: This study shows that TB patients in Tanzania spent most of their daily/monthly income either directly and/or indirectly on TB illness during treatment than on basic needs. This implies that there is a need for developing intervention strategies such as micro-finance models among TB patients to help them cope with economic consequences of tuberculosis illness.

PD-1137-29 Feedback from TB-affected households receiving a socio-economic intervention in Peruvian shantytowns: an acceptability assessment from the CRESIPT pilot study

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Background: Socioeconomic support is a key part of WHO's End TB Strategy. However, evidence is limited concerning which support elements (e.g. social, economic or both) will be acceptable to TB-affected families and achieve the greatest impact on TB control. During the pilot of a Community Randomized Evaluation of a Socioeconomic Intervention to Prevent TB (CRESIPT), we assessed the acceptability of a socioeconomic intervention for TB-affected households.

Methods: 282 TB-patients diagnosed by the Peruvian National TB Program in 32 shantytown communities of Lima, Peru, were recruited to the study. Patients were randomly allocated to the comparison arm (Peruvian NTP standard of care) or supported arm (standard of care plus socioeconomic intervention). The intervention consisted of social support activities (including health-post visits, household visits, TB educational workshops, and TB mutual-support clubs) and economic support activities (consisting of conditional cash transfers throughout treatment). At 24-weeks following treatment initiation, supported-arm participants completed a mixed-methods exit questionnaire to collect feedback on, and suggested improvements to, the social and economic support activities.

Results: 135 patient households were randomised to the support-arm of whom 127 engaged with the socioeconomic support intervention and 99 provided

feedback. Frequency of social and economic support activities rated as either 'good' or 'excellent' was: home visits 89/99 (90%); health-post visits 82/99 (83%); TB workshops 81/99 (82%); TB Clubs 79/99 (80%); and conditional cash transfers 83/99 (84%). Participant feedback and suggested improvements are summarised in the Table.

Table TB-affected household feedback on the intervention

Intervention activity	Positive	Aspect to improve on	Suggested improvement
Social support	1) Improved information and education. 2) Enhanced emotional and mutual support. 3) Increased self-confidence and esteem. 4) Motivating	1) Health-post, home visits, TB workshops, and TB Clubs too infrequent. 2) Lack of forewarning and difficulty coordinating times of social activities. 3) Workshops and clubs could be more dynamic.	1) Increase health-post visits to at least weekly and home visits, TB workshops and Clubs to twice a month. 2) Earlier formal invitation to activities followed-up by reminder phone call or text. 3) Include better audiovisuals: especially music and videos (including patient testimonies).
Economic support	1) Enabled participants to buy better food and cover travel costs to health-post for directly observed therapy or contact screening. 2) Cash transfers were encouraging and motivating.	1) Transfers not punctual, too infrequent, and not enough. 2) Complications of bank transfers included difficulty withdrawing cash, wasted visits when cash was not yet deposited, and hidden bank charges.	1) Increase cash transfer amounts, allow maximum 3-day wait to arrive, and provide cash transfers twice a month. 2) Inform household when cash transfers have arrived. 3) Allow participants to save up cash transfers (e.g. have some saved and then transferred at the same time).

Conclusions: In impoverished Peruvian shantytowns, a socioeconomic intervention had excellent uptake and feedback. Both the social and economic components of the intervention were found to be highly acceptable to the TB-affected households receiving them, who also provided useful suggestions to improve the intervention. These novel, TB-community led suggestions are being incorporated into refining the design of the ongoing CRESIPT study. The findings of this research provide important preliminary evidence to guide practical implementation of socioeconomic support for TB-affected households in line with global TB policy.

PD-1138-29 Not by choice but due to compromised financial situation. Compelling factors for choosing tuberculosis treatment in the public sector

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Background: The support of market economy, increased demand of quality health care and low credibility of public sector in providing health services has led to an overgrowth of private sector in providing treatment solutions for infectious as well as non-communicable disease. The objective of this paper is to correlate TB patient's socioeconomic conditions, treatment preferences with underlying reasons for choosing treatment in public or private settings.

Intervention: A cross sectional semi quantitative structured questionnaire based study was conducted among TB patients in two rural and two urban districts of Maharashtra. New and re-treatment adult pulmonary TB patients registered for treatment during 2nd and 3rd quarter of 2015 in 2 rural and 2 urban sites. A proportionate sample of 500 new TB cases (Rural=400, Urban=100) and 125 re-treatment (Rural=100, Urban=25) were interviewed capturing socioeconomic status (SES), type and number of health care provider consulted and related costs.

Results: 42% of patients treated within NTP were having SES of below poverty line (BPL) ($n=210$, 42%) in rural and 33% ($n=41$) in urban areas. Poor and lower middle class constituted 40% ($n=200$) in rural and 54% ($n=68$) in urban districts. First health care contact as a private provider constituted 67% in rural and 72% in urban areas. Average of 8.4 (Range 5-16) and 5.2 (Range 1-13) consultations were observed in rural and urban respectively. Average of 3.4 providers (Range 1-8) and 5.3 providers (Range 3-9) were being consulted before being diagnosed as TB in rural and urban setting respectively. Average total cost incurred by BPL, poor, lower middle class, upper middle class TB patients from day of onset of symptoms till they received treatment in NTP was proportionately 25%, 22%, 13% and 8% respectively of their annual household income. The decision of taking treatment in public health facility was solely based on non affordability of private treatment in 42% of rural and 52% of urban TB patients.

Conclusion: Trust is the main key that works in favor of private practitioners. Even though we have more than two decades of experience in PPM strategy, yet as of now we are out fashioned and still at large far away from involvement of ever growing private domain.

PD-1139-29 Preventing catastrophic costs: opportunities and barriers for reducing household TB-related costs

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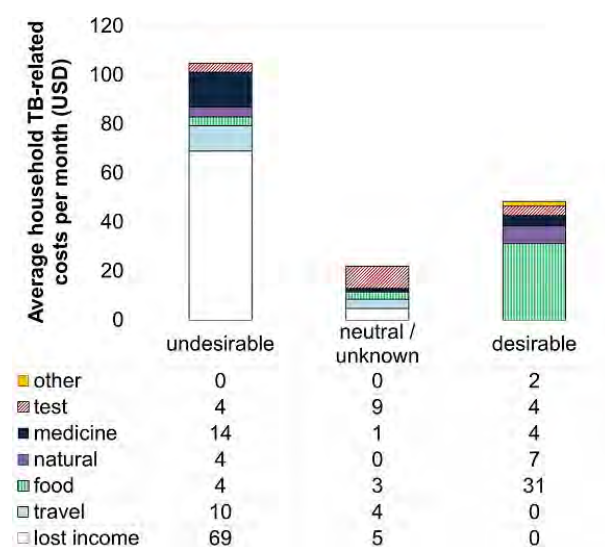
Background. Even when tuberculosis diagnosis and treatment are free, hidden costs can worsen poverty and future tuberculosis risk. High TB-related 'catastrophic' costs can cause as many adverse tuberculosis outcomes as multi-drug resistance. We studied illness-related expenses and patients' reasons for spending to inform the design of an intervention to reduce costs for tuberculosis-affected households.

Methods. Semi-structured patient interviews ($n=15$) were done in peri-urban health posts ($n=5$) in Callao, Peru with patients 0, 2 or 6 months after starting treatment for drug-susceptible tuberculosis. A costs-based questionnaire was designed to characterise tuberculosis-related household costs during the past month, reasons for these costs and the desirability they had to spend money on each cost. Once saturation of major themes had been reached, qualitative interview data was thematically analysed with quantitative analysis of patient costs.

Results. Cost categories included: lost income (an indirect cost), food, travel, medications, clinical tests or consultations, natural remedies and other costs. Excluding one patient with exceptional income, the average monthly total spent on all costs was 175 United States dollars (USD) per patient household, which constituted 13% of average household income. Most of these costs originated from lost income (74USD, 42%) with 0-6 months being taken off work. Food costs were second highest (38USD, 22%) mostly following nutritionist advice that was generally perceived positively. Travel costs (14USD, 8%) related to tests or consultations in larger health centres. Medications for symptoms (19USD, 11%) were bought from pharmacies, or after visiting a public health post, although some patients sought private consultations (16USD, 9%) which were perceived to provide faster or better care.

Conclusion. Lost income accounted for the largest proportion of patient costs and demonstrated high heterogeneity in health professional advice and patient behaviours. This highlights an opportunity to better support patients to return to work when appropriate, reducing catastrophic costs.

Figure Average TB-related costs and desirability (USD)



PD-1140-29 Cost-effectiveness of the community-based DOTS (CB-DOT) approach for treatment of tuberculosis in Afghanistan

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Background: Most of TB patients receiving direct observed treatment (DOT) from health facility are paying daily transportation cost to attend the health facility for taking TB medication. That incurs various costs to TB patients and their families and further devastates their economic status and could result in poor adherence to treatment. To reduce the cost Challenge TB (CTB) assisted Afghan National Tuberculosis program (NTP) to implement community based DOTS through local NGOs in 15 provinces of Afghanistan.

Methods: In first quarter 2016, CTB developed a questionnaire and sent to provincial CB-DOTS focal points of five randomly selected provinces (Nangrhar, Takhar, Khost, Baghlan and Faryab). They randomly selected 15 health facilities (HF) and 15 Community health workers (CHWs) in each province. They interviewed 260 (160 patients are taking DOT from HF while 100 patients taking DOT from CHWs) patients with active tuberculosis who registered for TB treatment. The study team compared the costs associated with two different approaches. We measured daily expenditure of a TB patient attended

health facility for DOT with TB patient taking DOT from CHWs during the initial phase of treatment.

Findings: The average cost for a TB patient attended HF for DOT was United States dollars (US\$) 10 (range 2-50) per patient in a month while average cost for a TB patient taking DOT from CHWs was less than US\$ one in a month. Average time a TB patient spent to attend HF for treatment was 97 minutes (range 40-360 minutes), however, this cost to a patient attended CHWs for treatment was 22.8 minutes (range 10 –120 minutes).

Conclusion: The health facility based DOTS approach appeared to be 10 times more costly than the Community based DOT approach to TB patients. The CB- DOTS approach brought TB services to door steps of TB patients that led to financial protection and could improve individual treatment outcomes. To support End TB strategy, The CB- DOTS full package program should be expanded to countrywide in Afghanistan and in similar settings elsewhere.

54. TB programme implementation and effectiveness

PD-1141-29 Tuberculosis patients in an Indian mega-city: where are they coming from and where are they diagnosed?

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Background: While 6054 smear-positive tuberculosis (TB) patients were diagnosed in the Revised National TB Control Programme (RNTCP) in Chennai, India in 2013, only about 3148 (52%) got registered for treatment in the city. We hypothesize that this gap is partly due to migration of patients to the city for diagnostic evaluation.

Methods: We collected data on all patients diagnosed with smear-positive TB at DMCs in Chennai in 2014 from the RNTCP. We analyzed these data to assess the distribution of smear-positive diagnoses across DMCs. We then visited 22 DMCs where >90% of Chennai's smear-positive patients are diagnosed and copied each site's DMC register for the month of May 2015. The address for all patients screened with sputum microscopy was coded by location and entered into a database. We estimated the proportion of chest symptomatics and smear-positive patients who live outside the city.

Findings: In the analysis 2014 data, out of 6135

diagnosed smear-positive patients, 3498 (57%) were diagnosed at just four DMCs located in tertiary care hospitals. Out of 50 total DMCs in Chennai, the 28 lowest volume DMCs collectively diagnosed < 10% of all smear-positive patients. In the analysis of May 2015 data, 570 of 3877 (14.7%) chest symptomatics and 53 of 350 (15.1%) patients with positive smears had an address outside of Chennai. At the four high-volume tertiary hospital DMCs, 425 of 1942 (21.8%) chest symptomatics and 38 of 213 (17.8%) patients with positive smears had an address outside of Chennai. At one of these high volume DMCs (Madras Medical College) 270 of 632 (43.3%) chest symptomatics and 20 of 41 (48.7%) smear-positive cases had an address outside of Chennai.

Conclusions: In India's fourth largest city, diagnosis of smear-positive patients is highly centralized, with just four DMCs making the majority of diagnoses. About one-sixth of all diagnosed smear-positive patients and one-fourth of patients diagnosed at tertiary care centers are from outside of the city—a finding with major implications for patient tracking and retention. The RNTCP should ensure strong coordination between tertiary DMCs in Indian megacities and the rural TB units where these patients are likely to take therapy.

PD-1142-29 Using geographical information systems for evidence-based programming and performance monitoring

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Background: Crowded and inaccessible residences hamper patient follow up to enforce treatment adherence. Geographical Information Systems (GIS) was used to determine TB hotspots and prioritized them for community linkage activities.

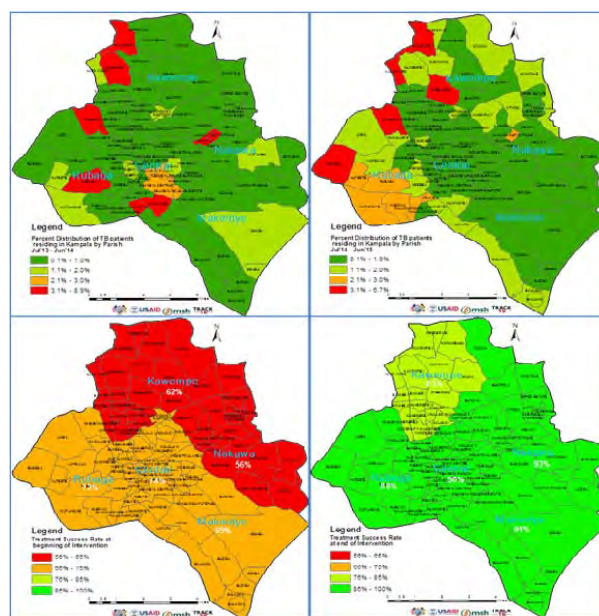
Intervention: USAID funded TRACK TB Project together with Kampala Capital City Authority (KCCA) used GIS software to develop maps of Kampala TB hotspots. The basic approach was as follows: physical addresses of 7,935 and 7,222 TB patients registered on TB treatment between FY2013/14 and FY2014/15 respectively were extracted from the TB unit electronic register. Data for 4261 and 4682 TB patients was cleaned and transferred to GIS software to develop the map of Kampala TB Hotspots. In addition to reporting, GIS data analysis was used to determine priority parishes for community awareness campaigns and outreaches on TB control, monitor quality improvement projects for community linkage facilitators, and spatial scan statistic was used to super-impose a circular window

on the maps and moving the centre of the circle over the area at different positions. This helped to identify parishes with the highest proportions of TB patients that were prioritized for community linkage activities.

Results: Community linkage activities namely patients follow up, community dialogues, outreaches, phone reminders, interrupter tracing and home visits led to improved cure/treatment success rates and linkage to HIV services as shown in the picture below.

Conclusion: GIS mapping, a cost effective and feasible intervention for evidence performance monitoring hence delivering patient centered care. It also improves communication, analysis and decision making.

Figure Kampala Hotspots



PD-1143-29 Tuberculosis prevention, diagnosis, and care in Manitoba, 2008-2010: a performance analysis

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Background: Manitoba has the highest incidence of TB of any province in Canada. First Nations (FN; one of three indigenous groups) in the province have the highest incidence of TB, followed by the foreign-born (FB). Canadian-born non-First Nations (CNFN) have the lowest rate. Two geographic regions of Manitoba had 87.9% of TB cases: The City of Winnipeg

($n=223$; 52.1%) and the Northern Health Region ($n=153$; 35.8%). This study analyzed TB program performance in Manitoba in terms of prevention, diagnosis, and care. The research questions included: 1) how is the Manitoba TB program performing? 2) does performance vary across ethnic-origin, geography, age, sex, and treatment history? 3) which performance indicators are measurable using Manitoba TB Registry data?

Methods: The study population included all 428 cases of TB diagnosed in Manitoba during the period of January 1, 2008 - December 31, 2010, as well as their contacts ($n=7,442$). Eight performance measures (PMs) were developed to analyze Manitoba TB program performance. Comparisons were made between FN, FB, and CNFN. Log-binomial and robust Poisson regression were used. For contact assessment data, a generalized estimating equations (GEE) approach was taken, clustering contacts within cases. We modelled the probability of each PM being met with results are presented as probability ratios (PRs).

Results: Treatment completion was highest amongst FN cases at 93.6%, although not significantly different from either CNFN or FB. Early diagnosis was lowest for CNFN at 50.0%, compared to 72.5% for FB and 69.5% for FN. HIV testing/reporting was low for all groups with 58.4% of cases having known HIV status. Re-treatment was highest amongst FN (6.4%). Paediatric TB was highest amongst FN, with 14.9% of cases being 14 years or younger. Assessment of contacts to infectious pulmonary cases was lowest for FB at 60.9% compared to 84.7% for CNFN and 81.9% for FN. We uncovered significant ethnic and geographic variation in TB program performance within Manitoba.

Conclusions: The performance measurement framework used in this study provided valuable information about TB prevention, diagnosis, and care in Manitoba and has contributed to TB program planning, serving as a catalyst for further investigation and action.

PD-1144-29 Assessing the quality of TB diagnosis, treatment and support services in private sector in India: a field-based case study

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Background: Private Practitioners in India treat more than half of tuberculosis patients. Private sector often has been blamed for non-standardized diagnosis, irrational treatment and major contributor to spreading drug resistance. Present study was conducted with an objective to assess quality of diagnosis, treatment service and support services for adherence provided

by private practitioners in Himachal Pradesh state in India.

Methods: In April 2015, a list of TB patients diagnosed, initiated on treatment and notified by private sector from 3Q2012 to 1Q2015 in Solan district in Himachal Pradesh was extracted from the web based system called Nikshay. After obtaining consent from patients, each one of them were contacted and interviewed using pretested checklist, medical records were also studied in details.

Results: Out of a total 126 notified by the private sector during the period, 90 patients and attendants of four deceased patients were interviewed. Cough (85%) was the most common symptoms reported by the patients, whereas near 1/3rd patients also reported fever along with cough. X-ray examination was done in most patients (79%), followed by blood investigation (74%), smear microscopy (55%), pleural fluid cytology (22%), and FNAC (1%). Patient reported a variable treatment history; 11% patients were on single drug, 28% patients were on two drugs, whereas near half of the patients were on three drugs regimen. Near one-fourth of patients were also given injections. No INH prophylaxis was given to eligible children. Treatment duration ranged from three months in 13% patients to >1 year in 8%. All doses were self-administered. 12 cases opted for taking DOTS in the public hospital. 22 (23%) cases were cured, 46 (48%) relapsed, 17 (18%) defaulted, 5 (5%) were failure and 4 (4%) died.

Conclusions: There are major limitations in the quality of diagnostic and treatment services by the private practitioners, which is reflected as a poor treatment outcome. Non-standardized diagnostics and inappropriate treatment regimen by PP are a major challenge for tuberculosis control and a cause for impending drug resistance. Each private practitioner must undergo sensitization training on Standard for TB care in India and adopt the same in practice.

PD-1145-29 Comparing tuberculosis management under public and private health care providers: Victoria, Australia, 2002-2014

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Background: Victoria, Australia, has low tuberculosis (TB) incidence and universal health care. TB cases are predominantly managed in the public sector, however a proportion do attend private healthcare providers. To provide recommendations to improve TB management we compared the healthcare received by TB cases in these sectors.

Methods: Retrospective cohort study: 2002-2014. Private healthcare provision was included as an independent variable in statistical analyses in addition to demographic, clinical, pathological and risk factor characteristics. Survival analyses were used to assess various time periods from symptom onset, healthcare presentation, investigations and treatment commencement. Multivariate logistic regression was used to analyse symptoms, laboratory tests, treatment regimens and treatment outcomes.

Results: Of 4,757 cases, 284 (6.0%) were seen exclusively by private healthcare providers, and 4,233 (89.0%) by public. In multivariate analyses private patients were significantly less likely to have genotypic TB diagnosis (Odds ratio [OR] 0.66, $P=0.009$, 95% confidence interval [CI] 0.48-0.90); and a sputum sample taken (OR 0.48, $P=0.003$, 95%CI 0.30-0.78), if there was pulmonary involvement; but were not significantly more likely to have a bronchoscopy (OR 1.11, $P=0.699$, 95%CI 0.66-1.85). The time between healthcare presentation and first specimen collection or chest X-ray was significantly longer (Hazard ratio [HR] 0.76 $P=0.001$, 95%CI 0.64-0.89) but the time between first positive chest X-ray or laboratory result and treatment commencement was not (HR 0.83 $P=0.168$, 95%CI 0.63-1.08). Patients attended private providers significantly sooner after symptom onset than public patients (HR 1.81, $P=0.002$, 95%CI 1.25-2.64) (symptom onset analysis restricted to 2012-2014) and, were significantly less likely to have a positive sputum (OR 0.40, $P=0.006$, 95%CI 0.21-0.77). Private patients were less likely to receive ethambutol (OR 2.30 $P=0.001$, 95%CI 1.41- 3.74), and more likely to be lost to follow up (OR 2.83, $P=0.012$, 95%CI 1.25-6.40). Improvements over time were observed for several disparities.

Conclusions: Our results indicate that patients may attend private healthcare providers earlier during their disease progression than those that attend public, however the disparities in TB treatment and outcomes between settings prompt the need for whole-of-sector strengthening approaches. These approaches may include educational engagement with private practitioners and improvements in private-to-public referral pathways.

PD-1146-29 Perspectives to end tuberculosis as a public health problem in Brazil

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Background: The World Health Organization has launched in 2014 the End TB Strategy that targets to reduce the incidence rate of the disease to less than 10/100 thousand population until 2035. In that sense, Brazil is developing a Plan, based on evidence, to achieve this target. The aim of this study was to analyze the trend and prospect of the TB incidence rate in Brazil.

Methods: An ecological study of timely series was developed through the data available in the Notifiable Diseases Information System from 2001 to 2014. Using Poisson regression, trend was estimated and associated variables with TB incidence rate were identified for Brazil. Thus, a multiple model was obtained to predict the incidence rate until 2035. This prediction was performed under two scenarios: 1) considering the stability in the values of the associated variables for TB incidence observed for 2014; and, 2) considering the improvement of these variables.

Results: The TB incidence rate presented a decrease of 2% per year (42.7 in 2001 to 34.1/100 thousand population in 2014). The independent variables associated were AIDS rate per 100 000 population (IRR=1.02; 95%CI 1.01-1.02), direct observed treatment (DOT) per 20% (IRR=0.99; 95%CI 0.98-0.99) and Family Health Strategy (FHS) coverage per 20% (IRR=0.96; 95%CI 0.95-0.98). The incidence rate will reach 25.7/100 thousand in 2035 if these determinants doesn't change after 2014. An increase in the FHS coverage and in the DOT (to 90%) and a decrease in the AIDS rate to 10/100 thousand would accelerate the rhythm of this decrease to a predicted value of 20.7/100 thousand until 2035.

Conclusions: Tuberculosis is still a public health problem in Brazil and to accelerate the reduction in the number of cases, the development of evidenced based Plans are necessary, especially regarding the strength of primary care, treatment adherence and AIDS control.

Figure Tuberculosis incidence rate. Brazil, 2001–2035

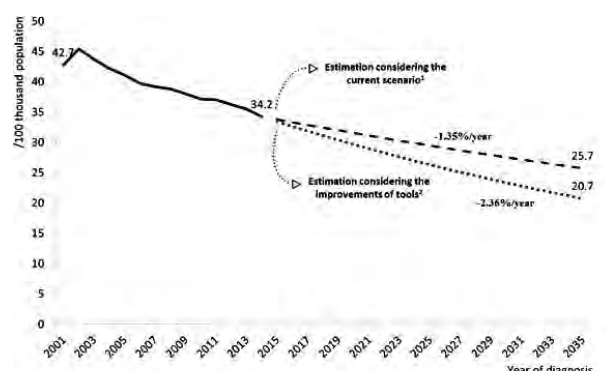


Figure 1- Tuberculosis incidence rate: observed and estimated values. Brazil, 2001 to 2035.

¹Poisson model if the current scenario of variables: year, AIDS incidence rate, Family Health Strategy and directly observed treatment, maintain stable to the values observed in 2014.

²Poisson model adjusted per year according to progressive improvements in the variables until 2035: AIDS incidence to 10/100 thousand population, Family Health Strategy and directly observed treatment to 90%.

PD-1147-29 Factors influencing smear non-conversion in patients with new smear-positive pulmonary tuberculosis, Antananarivo, Madagascar

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Setting: All the Diagnosis and Therapy Center in the city of Antananarivo in Madagascar.

Objectives: To determine : 1) the proportion of sputum smear-positive pulmonary tuberculosis cases who failed to smear convert at 2 months, 2) their treatment outcomes, and 3) their determinants factors.

Design: Cross-sectional retrospective study using medical files, tuberculosis registers and tuberculosis treatment records of new smear-positive tuberculosis patients, aged more than 14, registered from January to December 2014. Data were analyzed using Stata.11. The descriptive analysis was performed in relation to the study's objectives. Logistic regression models were used to identify factors associated to sputum smear non-conversion at the end of the intensive phase. Variables which have $P < 0.25$ were included in the first model, and those with $P < 0.05$ were retained for the last model after step by step descendant regression.

Results: Out of 1530 new smear-positive pulmonary tuberculosis patients treated during the study period, 1090 (71.2%) were included in the analysis. One hundred and twenty four (11.4% CI: 0.09-0.13) patients were identified as non-converted at the end of the intensive phase of treatment. As final out-

comes, 75% were successfully treated, and the failure rate was at 10.5% ($P=0.00$). Pre-treatment smears graded 3+ and 2+, losing weight and missing doses of anti-tuberculosis drugs during the initial phase of treatment were identified significantly as a risk factors ($P < 0.05$), AOR respectively=4 (IC95% [2.4-7.0]); 2 (IC95% [1.0 -3.6]; 6 (IC95% [4.0-9.8]) and 22 (IC96% [11.0-45.6]). Being 45 to 54 years old were also associated to delay in smear conversion ($P < 0.05$) AOR =2 (IC95% [1.3-3.6]).

Conclusion: Heavy initial bacillary load has been documented, as in our study, as an important risk factor of smear positive at the end of intensive phase of tuberculosis treatment. Many reasons can explain that. The limitation to this study is that analysis was based on data collected from patients' registers; therefore potential risk factors, such as clinical factors, co-morbid conditions, and HIV status, not found in the registers were not assessed. A prospective study including these other potential risk factors would be our perspective to complete our current data.

PD-1148-29 Geographic variation of tuberculosis case notification in two regions of Ethiopia and its implication on TB program management

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Background: Variations in the Ethiopian tuberculosis (TB) epidemiology was noted in the national TB prevalence survey that showed a higher rate of bacteriologically confirmed TB cases among the pastoralist population and lower rate in urban clusters. The objective of this analysis was to assess the variation in case notification rate across different zones using data from the routine health information system.

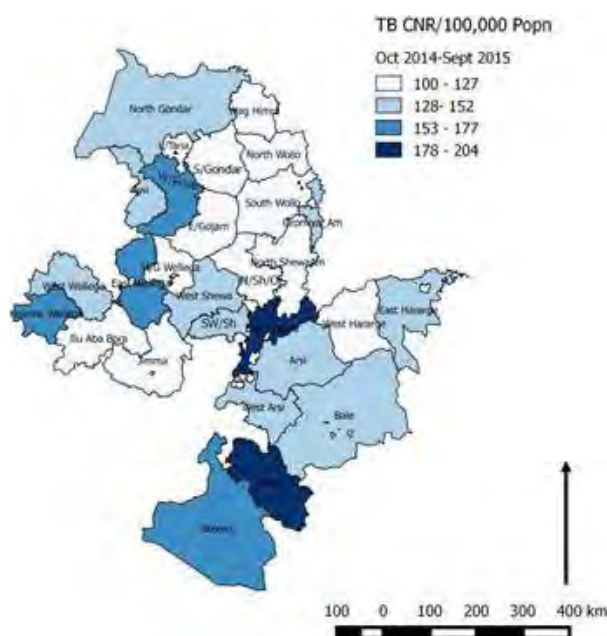
Methods: One year data on case notification was compiled and case notification rate (CNR) was calculated for each zone in two regions of Ethiopia. Zones were classified in to four categories based on their CNR. The data was transferred to Quantum GIS software and the software was used in the mapping of zones.

Results: TB case notifications were heterogeneous among the 28 zones. Two zones (both in Oromia Region) were in the highest range (CNR range of 178-204/100 000) while 4 zones were in the second highest range (CNR range of 153-177/100 000). Ten zones had the lowest range of case notification: 6 in Amhara and 4 in Oromia regions (CNR range of 100-127/100 000). The lowest CNR was 102 per 100 000 recorded in two zones while the highest CNR of 203

per 100 000 was recorded in one zone in comparison with the project average CNR of 135 per 100 000. The two zones that had the highest TB case notification are peculiar in some aspects: one is a pastoralist area that is also inhabited by migrant workers while the second one is a corridor with relatively higher HIV prevalence.

Conclusion: The heterogeneity in case notification could be ascribed to real difference in the prevalence of TB, variability in case detection efforts, or to other factors fueling the transmission of TB in the different geographic areas. We recommend prioritization and focused intervention in geographic areas with higher case notification.

Figure Geographic distribution of all forms of TB



PD-1149-29 False positivity in old and new definitions of sputum smear-positive pulmonary tuberculosis at various levels of true tuberculosis prevalence

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Background: Treatment of false positive cases is a risk factor for drug resistance and has financial implication in resource poor settings. With an aim to identify and treat the most infectious form of TB (sputum smear-positive pulmonary cases), a higher sensitive definition 'pulmonary case with one or more initial sputum-smear-examinations (SSE) positive for acid-fast bacilli (AFB)' has been adopted which holds good in high prevalence and functional external quality assurance (EQA) setting. However, lowering of TB

prevalence in developing countries and reduced specificity could result in higher false positive cases. This study models to identify the level of true prevalence of pulmonary TB among suspected cases that could require further diagnostic aid for accurate diagnosis.

Methods: Using epidemiological principle for estimation of sensitivity and specificity in multiple tests the expected false positive rates for two-SSE (new-definition) and three-SSE (old-definition) were estimated at various expected levels of true prevalence of pulmonary TB among suspected cases. Assumptions [sensitivity (spot-sputum-sample microscopy=0.85, morning-sputum-sample microscopy=0.95), Specificity=0.97] were considered based on literature. The decision for diagnostic aid was determined at false-positive-rate of 33% or more.

Results: Missing cases (False-Negative) remain low and constant (old-definition: 3.53%; new-definition: 0.75%) irrespective of prevalence level. New definition yields higher false-positive rates than old definition. At prevalence levels 0.1%, 1%, 5%, 10%, 15% and 25% the false-positive rates were 98%, 85%, 53%, 35%, 25% and 15% respectively for case identification by new definition; and 73%, 21%, 5%, 2% and 1% respectively for old definition.

Conclusions: The performance of new case definition at true prevalence $\leq 10\%$ (10,000 per 100 000 suspected population) is limited considering high false-positive rates ($>35\%$). In view of global lowering trend of TB prevalence, additional other diagnostic aid is recommended to deter high-false positive rates in developing country settings.

PD-1150-29 Social determinants of non-adherence to tuberculosis treatment in selected municipalities of Buenos Aires, Argentina

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Background: The aim of this study was to identify the social determinants of adherence to tuberculosis treatment, at different levels in selected municipalities of Buenos Aires, Argentina.

Methods: An ecological study was conducted in selected municipalities, to identify spatial distribution patterns of the proportion of non-adherence (analysis of spatial correlation); and a cross-sectional study with a model of hierarchical analysis, conducted in Buenos Aires, Argentina. Data was collected through a questionnaire and the characteristics of the area based on National Population Census were analyzed. The social determinants' analysis was performed using multiple logistic regression (2-level hierarchical model).

Results: The final results of the ecological study show higher incidence rates of non-adherence to treatment in areas with a lower proportion of the population that does not make pension contributions, in areas with a higher proportion of households with UBN as subsistence capacity and in areas with a higher proportion of households that do not have public transport within 300 meters. The final model of the hierarchical analysis shows that at the individual level male patients had 3 times higher risk of non-adherence to treatment. Not having water supply at home increased 4 times the risk of non-adherence, compared with homes that have water supply. In households where the head of household had no health coverage, the risk of non-adherence to treatment increased almost 6 times. Patients who used more than one means of transport to attend the health service had nearly 7 times the risk of non-adherence to treatment than those who used only one mean of transport. At the area level, areas with a higher proportion of households with UBN as subsistence capacity presented more than triple risk of non-adherence. Areas with higher proportion of households without natural gas network had a lower risk of non-adherence. Finally not having flush toilet increased more than 5 times the risk of non-adherence.

Conclusions: In conclusion, adherence to tuberculosis treatment is part of a complex multidimensional process. The results show that there is an influence of social and economic variables for non-adherence to tuberculosis treatment, both individually and geographically (area).

PD-1151-29 Can the number of patients with presumptive tuberculosis lost in the general health services in Pakistan be reduced?

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Background: The frequency of patients with presumptive tuberculosis (TB) who are not investigated by sputum smear microscopy is unknown in Pakistan.

Methods: Using a simple intervention comparing patient and laboratory registers, patients with presumptive TB were identified in two districts from July to December 2013, a list of missing patients was prepared and the patients traced.

Results: The intervention significantly reduced the number of patients with presumptive TB lost, from 8.5% before the intervention to 6.9% after. A

systematic comparison of out-patient and laboratory registers, followed by tracing missing persons, can reduce the proportion of patients with presumptive TB lost before diagnosis.

Conclusions: A simple comparison of out-patient and laboratory registers on a routine basis and tracing lost patients with TB symptoms can be effective in minimizing loss to follow-up of patients with presumptive TB. Such a strategy should be replicated and tested elsewhere, complemented by other studies where improved coverage of testing for presumptive TB cases leads to improved diagnosis and treatment.

PD-1152-29 What is the time from symptom onset to the initiation of treatment for tuberculosis patients in Afghanistan?

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Background: Afghanistan is home for 60,000 new TB patients in a year. In 2015, National Tuberculosis program (NTP) notified 62% of estimated TB cases owing to delayed diagnosis. There has not been any study to show the time interval from onset of TB symptom till diagnosis and treatment in Afghanistan. The aim of this study was to identify that how much time it takes for TB patients from symptoms till diagnosis.

Methodology: This was a cross sectional study used a random cluster sampling of health facilities from 12 provinces that represents factors like security, culture and geographic location. The study team reviewed records of TB patients in the cluster that diagnosed and registered at public and private health facilities. Researchers collected data from TB register of health facilities.

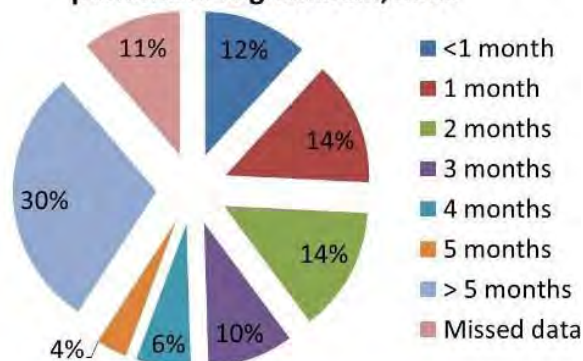
Results: Study team reviewed records of 3,221 patients that started treatment in 2014. Of them, 30% remained symptomatic until five months, 12% diagnosed within one month, 14% diagnosed between 1-2 months and for 10% it took three months till diagnosis and treatment (Graph-1). Briefly, health facilities diagnosed 26% of patients within one month of symptom onset, 50% till three months, 60% until five months and rests afterwards. Further, 42% male and 36% female TB patients diagnosed within two months and 30% male and 35.3% female diagnosed after five months of symptoms onset. Also, there was no difference in time from symptoms onset until diagnosis between pulmonary and extra pulmonary TB patients.

Conclusion and recommendation: Among study subjects, there was an unacceptably delay from onset of symptoms and treatment initiation. Also, female

patients stayed symptomatic longer compared male patients. Thus, we recommend strengthening health system to detect and diagnose TB earlier and differential diagnosis of TB among chest symptomatic clients at public and private facilities.

Figure Time interval from symptom onset

Time interval from TB signs and symptoms initiation till diagnosis and treatment of TB patients in Afghanistan, 2015



55. TB contact tracing and latent TB infection

PD-1153-29 Prevalence of latent tuberculosis infection in the community by meeting venue

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Background: In high-burden areas, indoor congregate settings, such as public places, are the main source of tuberculosis transmission. However, specific venues where tuberculosis transmission occurs in the community is poorly understood. Comparison of latent tuberculosis infection (LTBI) rates in several distinct congregate locations has never been performed in the same setting. Tuberculosis control efforts will benefit from a more venue-specific targeted interventions.

Methods: From 2009 to the present, we conducted a cross-sectional study in patients with active tuberculosis in Kampala, Uganda. Trained social scientists/health workers interviewed subjects with tuberculosis disease to assess the nature of their relationship to their community contacts and to obtain a list of the usual meeting places for each of their contacts. A

tuberculin skin test (TST) was done on each contact, and LTBI was defined as a TST induration ≥ 10 mm.

Results: We analyzed 240 community contacts of 58 tuberculosis cases. Each tuberculosis case had an average of four traced community contacts (range 1–12) in their social network. The median age of the contacts was 25 years (range 1–61 years) and 55% of them (131/240) were male. Their most common place of meeting was the workplace (33%), followed by the home of the tuberculosis case (27%), friend's home (11%), relative's home (10%), trading center/shop/kiosk (6%) and bars (4%). The prevalence of LTBI among community contacts was higher when the usual venue of meeting was a bar (5/10, 50%), workplace (33/79, 42%) or trading center/shop/kiosk (6/15, 40%), and lower when the contact was in a home of a tuberculosis case (24/65, 37%), a friend (9/26, 35%) or relative (7/25, 28%).

Conclusions: In community contacts of tuberculosis cases, certain public settings appear to be associated with a substantial risk of LTBI. A prospective longitudinal study is currently underway to determine whether these venues, and the frequency and duration of the meeting, increases the risk of incident tuberculosis infection, as a measure of community transmission.

PD-1154-29 Risk of tuberculosis in Germany

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Background: Few individuals latently infected with *M. tuberculosis* (LTBI) progress to active disease. We investigated risk factors for LTBI and active pulmonary tuberculosis (PTB) in Germany.

Intervention: Healthy household contacts (HHCs), tuberculosis exposed health care workers (HCWs) and PTB patients were recruited at 18 German centres. Interferon- γ release assay (IGRA) testing was performed. LTBI risk factors were evaluated by comparing IGRA-positive with IGRA-negative contacts. Risk factors for tuberculosis were evaluated by comparing PTB patients with HHCs.

Results: From 2008–2014, 603 HHCs, 295 HCWs

and 856 PTBs were recruited. LTBI was found in 34.5% of HHCs and in 38.9% of HCWs. In HCWs, care of coughing patients ($P=0.02$) and longstanding nursing occupation ($P=0.04$) were associated with LTBI. In HHCs, predictors for LTBI were a diseased partner (odds ratio 4.39), sexual contact to a diseased partner and substance dependency (all $P < 0.001$). PTB was associated with male sex, low body weight ($P < 0.0001$), alcoholism (15.0% vs. 5.9%; $P < 0.0001$), glucocorticoid therapy (7.2% vs. 2.0%; $P=0.004$) and diabetes (7.8% vs. 4.0%; $P=0.04$). No contact developed active tuberculosis within 2 years follow-up.

Conclusions: Positive IGRA responses are frequent among exposed HHCs and HCWs in Germany and are poor predictors for the development of active tuberculosis.

PD-1155-29 Yield of contact investigation under programmatic conditions in rural Namibia

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Background: TB is a significant public health problem in Namibia, with an estimated incidence rate of 561 cases/100 000 and a case detection rate of 66 % in 2014. 9,882 cases of TB were notified in the same year, with an HIV prevalence of 44% among TB patients. Like in most countries, contact investigation for TB is recommended in the guidelines but is poorly implemented and erratically documented. In practice, health care workers prioritise household and other close contacts who can present to health-care facilities. This assessment was the first aimed at quantifying the yield of contact investigation for TB in the routine system in Namibia

Intervention: A review of TB registers, treatment cards and IPT registers was conducted at 44 health facilities in Oshikoto and Kunene, two rural regions of Namibia for a period of 8 months in 2014. Where possible, contacts were asked for common TB symptoms, cough, night sweats, fever and weight loss as well as age and HIV status.

Results: 664 index TB cases were identified during this period, with a total of 299 contacts who had documented investigation. Of the 299, 44 (15%) were children under the age of 5 years and 13 self-reported having HIV. Seven of the child contacts; one of the HIV positive contacts and 50 of the other adult contacts had symptoms compatible with TB. A total of 23 (8%) of contacts, including three children under 5 were diagnosed with active TB during the period.

This represents a prevalence of 7,692 cases of TB per 100 000.

Conclusions: Contact investigation is still seen as a time-consuming add-on for already overworked health workers, hence the low rate of contacts investigated. The prevalence of active TB among close contacts is very high, justifying the need to focus on close and household contacts even in rural Namibia. This is particularly important given the high HIV prevalence and the significant TB burden in Namibia.

PD-1156-29 Yield of facility-based verbal screening amongst household contacts of patients with multidrug-resistant tuberculosis in Pakistan

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Background: Household contacts of multidrug-resistant tuberculosis (MDR-TB) patients are at a high risk of getting infected with TB/MDR-TB, therefore symptomatic or vulnerable individuals should be screened and treated early.

Methods: A cross-sectional study was conducted among household contacts of MDR-TB patients in three high-burden sites in Pakistan from July 2013 to June 2014. MDR-TB index patients were asked to provide a list of all members of their household and were asked whether any of them had TB symptoms such as productive cough, fever, weight loss and night sweat ('facility-based verbal screening'). Symptomatic contacts were defined as presumptive TB cases and were invited for investigations at the facility. Those who did not come were paid a home-visit. Confirmed TB/MDR-TB patients were registered in the nearest treatment facility.

Results: Of 209 MDR-TB index patients, 1467 household contacts were identified and screened, 95 of them children < 5 years. Of them 172 (12%) were symptomatic. Most common symptoms were cough (91%) and fever (62%). Fifty-eight (34%) symptomatic contacts were not investigated. Out of total contacts 56 (3.8%) diagnosed with TB, among them 54 (96%) with MDR-TB and 2 (4%) with drug-susceptible-TB. The number needed to screen to identify a new MDR-TB case among adult household contacts was 27 and among presumptive adult and pediatric TB contacts was three. All 56 confirmed patients were registered for treatment

Conclusions: Screening household contacts of MDR-

TB index cases may be considered feasible and very high yield, especially in high-burden settings like Pakistan. The number of presumptive TB contacts needed to screen to find a new MDR-TB case was unusually low, indicating a very effective strategy that may be scaled-up. The screening and management of adults and children who live with patients with any form of TB is a major priority in the effort to end TB.

PD-1157-29 Innovative geographic information systems (GIS) based screening for tuberculosis contacts in household and community contacts in Pakistan: how effective is it?

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Background: Pakistan ranks fourth globally among the 22 high TB burden countries with 64% of case detection rate and It accounts for 61% of the TB burden in the Eastern Mediterranean Region (WHO). There is a need to enhance TB case finding to meet MDG targets.

Setting: Active case finding through contact screening using GIS software in 3 cities in Punjab Province i.e. Lahore, Faisalabad and Rawalpindi and the Capital Territory utilizing all SS+ notified cases as index cases registered at BMU's.

Aim: The study aims to determine the effectiveness of community and household contact tracing through outreach using GIS.

Methods: Project funded through TB Reach wave 3 was focusing on contact screening is being carried out within household and a diameter of 100m around each index case using GIS Technology and therefore strengthen current contact screening strategy adopted by NTP. Household contacts, i.e. those normally resident or sharing the same airspace, were verbally screened initially, followed by a widening circle screening of close community contacts. The coordinates of the household were entered into a GIS database via a mobile phone link. There were 50 field officers trained for this project. All the TB presumptive found from the screening were subjected to smear microscopy; those found positive are registered. However, those found negative were subject to Gene Xpert. Gene Xpert positive cases with or without rifampicin resistance were also registered for treatment at the respective sites. TB presumptive aged less than 15 years identified were referred to child TB managing sites for diagnosis and treatment and were followed up.

Results: From July 2013 to 7th April 2015, total of 617,642 individuals were screened, among them 74,329 are household and 543,313 are community based, total TB presumptive found 19,257 (household=4326, community=14931), in which smear

positive cases are 2988 (community=2254, Household=734), gen expert positive cases are 271, MDR cases are 39, child referred are 4875 and total registered cases are 3406.

Conclusions: Contact screening among community is proved to be effective in addition to household screening for early case detection and to limit spread of disease.

PD-1158-29 Correlation of childhood TB case notification with bacteriologically confirmed pulmonary TB case notification: results from two regions of Ethiopia

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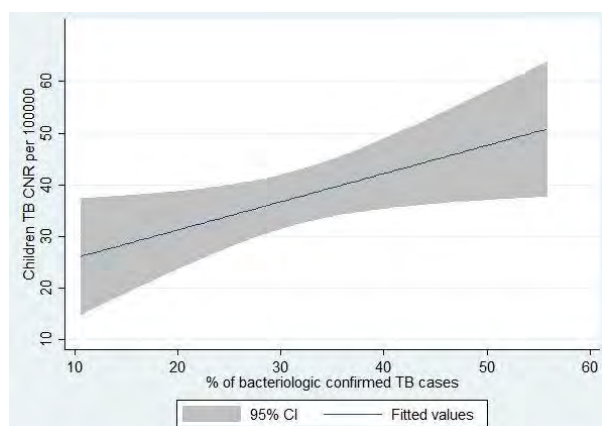
Background: With the very limited resources available, knowing the clustering of childhood TB cases is a good strategy to prioritize and allocate resources efficiently. The objective of this analysis is to assess the relationship between the burden of bacteriologically confirmed TB cases and childhood TB case notification rate (CNR).

Intervention: Since 2011, the USAID-funded Help Ethiopia Address the Low Performance of TB (HEAL TB) Project supported health facilities in Amhara and Oromia in building local capacity to diagnose and manage childhood TB cases. Linear regression analysis was made. The zonal level childhood TB CNR and percentage of bacteriologically confirmed TB cases were categorized in to four quartiles and presented in a map.

Results and lessons learnt: There was positive correlation between childhood TB CNR and percentage of bacteriologically confirmed TB cases ($r=0.37$). A 10% rise in bacteriologically confirmed pulmonary TB cases results in 5.5% increase in childhood TB CNR (Coefficient 0.55, 95% confidence interval, 0.063-1.03, $P<0.05$) (Figure). Mapping also showed that the majority of zones with higher quartile score in bacteriologically confirmed pulmonary TB cases also had higher quartile score in childhood TB CNR. The routine data helped us to understand the link and generate evidence for decision making.

Conclusion: There is a direct link between childhood TB case notification and burden of bacteriologically confirmed TB. Interventions like contact investigation of bacteriologically confirmed TB cases and childhood isoniazid preventative therapy needs to be given higher emphasis in zones with higher burden of bacteriologically confirmed TB.

Figure



PD-1159-29 The yield of tuberculosis contact screening in Ethiopia: comparing contacts of bacteriologically confirmed and clinically diagnosed index TB cases

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Background: Ethiopian National TB program adopted TB contact screening for all forms of TB cases including the clinically diagnosed index TB cases (Smear negative pulmonary TB and extra pulmonary TB cases). However the results from the intervention are not yet systematically analyzed. We present the comparative yield of TB among contacts of bacteriological confirmed and clinically diagnosed index TB cases.

Intervention: USAID-funded Help Ethiopia Address the Low TB performance (HEAL TB) project supported the training of health workers and provision of regular mentorship in Amhara and Oromia regions. All enrolled TB cases are informed to bring their contacts to a health facility for screening. The report covers the performance during January-September 2015.

Result and lessons learnt: A total of 105 954 TB contacts (98% of those registered) were screened TB. The majority of the screened contacts (80.5%) were aged above 5 years. A total of 1992 (1.88%) presumptive TB cases were identified, of which 398 (0.38%) TB cases were diagnosed: 289 (0.7%) and 109 (0.17%) were among bacteriologically confirmed and clinically diagnosed TB contacts, respectively (Table). The TB case notification rate among bacteriologically confirmed TB cases contacts was 686 per 100 000 which is fourfold the yield of TB among clinically diagnosed TB contacts ($P < 0.05$).

More than half of TB cases identified among contacts of bacteriologically confirmed TB cases were also bacteriologically confirmed; whereas 63% of TB cases identified among contacts of clinically diagnosed TB cases were also clinically diagnosed TB cases. There was no significant regional variation in the yield of TB ($P > 0.05$).

Conclusion: The yield of TB among contacts of bacteriologically confirmed index TB cases was more than four times as compared with clinically diagnosed TB cases. However, the yield found through contact screening of clinically diagnosed cases is three times higher than the case notification rate in the general population.

Table Yield of TB among contacts of bacteriologically confirmed and clinically diagnosed index cases

Indicators	Bacteriologically confirmed index case <i>n</i> (%)	Clinically diagnosed index case <i>n</i> (%)	Total <i>n</i> (%)
Contacts screened for TB	42 136 (98.44)	63 814 (97.98)	105 950 (98.2)
Presumptive TB identified	1044 (2.48)	948 (1.49)	1992 (1.88)
TB cases identified (% among presumptive TB cases)	289 (28.00)	109 (11.50)	398 (19.98)
TB case notification per 100 000 contacts (95%CI)	686 (611-769)	171 (141-206)	376 (340-415)

PD-1160-29 Body mass index and TB incidence: a consistent dose-response relationship among adult household contacts

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Background: Population nutritional status is an important social determinant of tuberculosis incidence. A previous review demonstrated an inverse, log-linear relationship between body-mass-index (BMI) and incidence. In order to further characterise this relationship, we prospectively evaluated a cohort of household contacts in Callao, Perú.

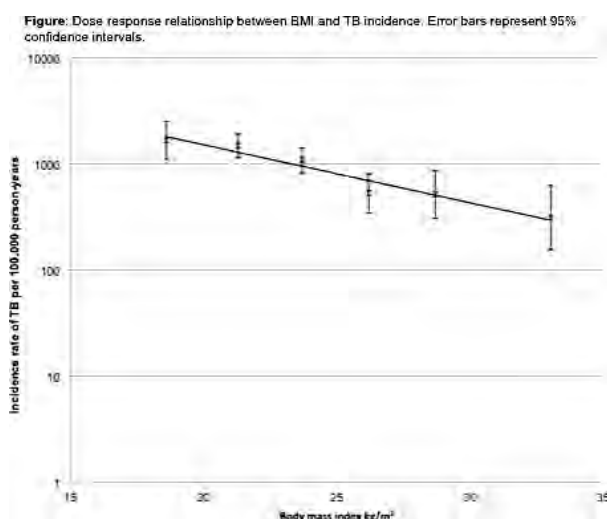
Methods: Between 2002-2006 we recruited 2,017 contacts aged ≥ 15 years of 715 patients with laboratory confirmed, pulmonary tuberculosis. Height and weight were measured at baseline and BMI calculated. BMI was adjusted for contacts aged 15-18 years using the WHO BMI-for-age charts.

Contacts were followed up for incident tuberculosis with collaboration from the National Tuberculosis Programme (NTP) for a median 11 years. In addition, we performed three prevalence surveys during which we offered sputum smear-microscopy and culture testing to all contacts. We calculated incidence rates with 95% confidence intervals across categories of BMI and fitted a linear trend line against incidence. We subsequently estimated the incidence rate ratio for a one-unit increase in BMI using the Mantel-Cox method.

Results: 172 contacts developed tuberculosis during 18,988 person years of follow up equating to an incidence of 906/100 000 person-years. BMI was normally distributed with a mean of 24.3kg/m² (SD=4.3) and a range of 17.8-46.4. We demonstrated an inverse, log-linear, dose-response relationship between BMI and tuberculosis incidence (Figure). The incidence rate ratio for a one-unit increase in BMI was 0.90 (95%CI 0.86-0.93; $P < 0.0001$).

Conclusion: In this prospective cohort study of adult household contacts exposed to tuberculosis patients the risk of tuberculosis increased by 10% for each one-unit reduction in BMI. Our results from this high-burden setting corroborate previous findings and suggest that being overweight may in fact reduce tuberculosis risk. In undernourished household contacts, NTP prevention interventions aiming to ensure adequate nutrition and weight gain may reduce tuberculosis incidence as well as benefit overall health and wellbeing.

Figure BMI and TB incidence



56. As a team everybody achieves more: innovations to strengthen TB case finding

PD-1161-29 Intensifying TB case finding in hospital

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Background: TB incidence in Cambodia is estimated at approximately 61,000 per year and case notification is about 39,055, thus about 22,000 (36%) are missing. Approximately one third of presumptive TB patients referred to hospitals never make it there. A study in China has shown that monitoring hospital reporting and referrals and active follow-up of reported patients has increased the case notification of smear positive TB by 33%. In Cambodia, most hospitals do not have systematic TB symptom screening at triage and referral for work up diagnosis is not systematically tracked.

Intervention: Project aims to improve TB case detection via screening of presumptive TB patients at triage and in-patient wards. The project approach includes a baseline assessment of TB case management practices, health care workers' knowledge on TB and flow of patients. A meeting is held with key personnel and the hospital director to introduce the activities and decide on key personnel and specific work. Four key TB symptoms have been included in both triage and in-patient medical record forms to remind physicians to identify presumptive TB patients. Cough triage and 'FAST' approach are introduced in the triage area. A referral process is strengthened to assure diagnosed patients continue treatment after hospital referral to peripheral health centers (HC). A feedback mechanism is created between hospitals and HC and reviewed on a monthly basis to ensure patients reached the HC.

Results: In 2015, the approach has been implemented in 5 hospitals, and number of patients screened for TB and TB case notification have significantly increased in each quarter as presented in table below:

Conclusions: Inclusion of four TB symptoms into exiting patient medical record forms, introduction of TB cough triage, and strengthening the referral system have improved yield of TB case notification in the hospital; the approach is operationally feasible and replicable.

Table Quarterly case notification

Quarterly	Number of patients screened for TB	Number of TB case notifications
1	42 007	455
2	43 719	465
3	48 389	579
4	37 782	661

PD-1162-29 Active TB case finding in the private sector in the Eastern Development Region of Nepal

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Background and challenges to implementation: Low case detection and notification are two of the major challenges facing the National TB Program (NTP) Nepal. The private sector is believed to treat a third of Nepal's TB patients, yet the vast majority of these patients are never notified to the NTP. With support from TB REACH, International Organization for Migration in collaboration with the NTP and Sahara Nepal, implemented active case finding (ACF) in private facilities in six districts of Eastern Nepal.

Intervention or response: One Hundred private health facilities were selected with NTP and coordination and advocacy meetings were held to motivate health staff to become involved with the project. Community health workers were recruited and trained to screen people visiting outpatient departments (OPDs) at private hospitals for symptoms of TB. Individuals with a positive screen were asked to submit sputum specimens for testing by smear microscopy (SM). Smear-negative patients were then examined by chest x-ray (CXR) and the Xpert assay if the CXR was abnormal. Patients with active TB were treated at NTP facilities.

Results and lessons learnt: A total of 139,370 OPD patients were verbally screened, resulting in the identification of 15,996 (11.47%) people with symptoms and the collection and testing of 14,913 sputum samples for testing with SM. 1209 (8%) smear-positive TB patients were identified. A further 1,064 individuals had an abnormal CXR and were tested by Xpert, resulting in the detection of 269 MTB-positive patients, a 25% increase over SM alone. All detected patients were notified and started treatment. The case notification was improved in the evaluation population. Over 500 additional cases were notified compared to baseline.

Conclusions and key recommendations: Large number of patients visit small private clinics/pharmacies due to low consultation fee. Subsequently, more TB cases were detected in such settings. Big hospitals and clinics having their own laboratories were reluctant to refer the patient because they had fear of losing patients (income). Many private practitioners were not aware of NTP policy on TB diagnosis and care and not following it. The results show that active case finding intervention in private sector can be implemented to increase TB case detection.

PD-1163-29 Improved TB case notifications by engaging the private sector through Private Provider Interface Agency in Mumbai, India: 2013-2015

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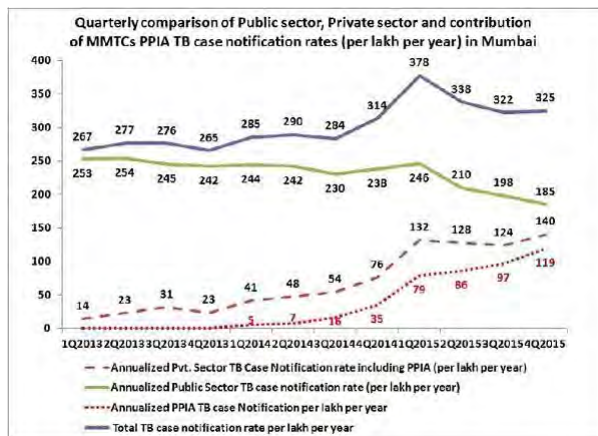
Background: Annually 30 000 TB cases get registered for treatment in Mumbai under the Revised National Tuberculosis Control Programme (RNTCP). However, though there are no reliable estimates, equal number seek TB treatment in private sector. In May 2012 India declared TB a notifiable disease. Further, in response to the report of total drug-resistant TB patients in Mumbai during 2012, Municipal Corporation of Greater Mumbai (MCGM) implemented Mumbai Mission for TB Control (MMTC). One crucial activities was involving private providers through the Private Provider Interface Agency (PPIA) seeking to create a 'network' of formal/informal healthcare providers to offer subsidized TB care and Standards of TB Care in India.

Methods: The present study examined trends of TB notification rates during 2013-15 in both, the public sector and the private sector including trends for private sector notifications through PPIA. Retrospective records were reviewed and ecological correlations made to explain some unexpected variations in total case notification trend.

Results: The private sector TB case notification rate in Mumbai increased from 14 to 140 per lakh per year during 1Q2013 to 4Q2015 (Figure 1). The percentage contribution of TB cases notified through PPIA out of total TB cases notified in private sector has increased from 13% to 85% during 1Q2014 to 4Q2015. The peak of 1Q2015 was correlated to the backlog entries. The total case notification increased by >100 per lakh per year during 1Q2013 to 1Q2015. However, after 1Q2015 there is a decrease in public sector notifications owing to administrative decisions regarding case registration following internal evaluations of two Mumbai wards.

Conclusions: In conclusion effective involvement of private sector through an interface agency has helped MCGM notify more than 11,000 additional TB cases during 2015, while providing for free or subsidized TB services to patients and behavior change to follow Standards of TB Care among private providers.

Figure TB notification rates, Mumbai 2014-15



PD-1165-29 Community-based active case finding: a strategy to increase TB case detection in Mandalay, Myanmar, 2012-2015

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Background: Tuberculosis (TB) case detection rate in Myanmar is reported to be 70% in 2014 which is comparable to other TB high burden countries. However, poor and vulnerable populations who are at risk of TB are not always accessible to available TB diagnosis services, which results in late diagnosis and treatment, high mortality and continued transmission of infection. Involvement of the community, community health workers and private partners are crucial parts of the new post-2015 Global TB Strategy.

Methods: We reviewed routinely collected data at the township health centers between 2012 and 2015 in seven townships in Mandalay, Myanmar.

Setting: The Union Program to Increase Catchment of TB Suspect have implemented community based active case finding (ACF) activities in slums, factories and industrial zones in seven townships in Mandalay, Myanmar since 2012. The activities included community health education, screening of TB contacts and risk groups (PLHIV, DM, previously treated TB patients), mobile chest X-ray clinic, advocacy with pharmacists and general practitioners for referral of presumptive TB patients, and facilitation of TB diagnosis investigations (sputum smear microscopy, chest X-ray and GeneXpert test) to enhance early detection of TB case. Trained community based

volunteers reached out to the community for ACF activities. People with presumptive TB were identified and referred to township health centers for TB diagnosis and treatment. We aim to determine the number referred and number diagnosed as TB.

Results: Among 36,873 presumptive TB patients referred to township health centers and investigated, 5,653 (15%) were diagnosed with TB. Of them, 43% were bacteriological confirmed TB. Most of the referrals were from community volunteers (54%) or self-referrals (33%) after community health education. Contacts of TB patients constituted 75% of the referrals. There was higher yield of TB among males (20%), children aged < 5 years (25%), people referred from general practitioners (35%), diabetes mellitus patients (28%), people who had history of TB (28%) and people living with HIV (30%).

Conclusions: Community-based ACF was effective in detecting TB cases. Future research should examine the cost-effectiveness of such approaches.

PD-1166-29 Can repeated visits and examinations of contacts of pulmonary TB cases yield additional TB cases within households? Southern Ethiopia

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Background: The objective of the study is to determine the incidence of additional TB cases among HHCs of smear-positive pulmonary tuberculosis (PTB+) patients through repeated visits and examinations in Boricha district, Southern Ethiopia.

Methods: Retrospective record review of PTB+ index cases treated between November 2010 and March 2015; and their HHCs were conducted. Health extension workers regularly visited households of index cases as part of routine activities and screened symptomatic cases. Households of all index cases were revisited for final screening and examination from April-June 2015. TB cases diagnosed among HHCs during the first contact tracing visits were considered prevalent cases. The periods between the index case started treatment until the date secondary cases diagnosed and the last screening was calculated. Diagnosis of TB was made using smear-microscopy and/or X-rays.

Results: 393 index cases and 1,698 HHCs were screened. During the first household visits, 47 HHCs were symptomatic and 3 (6.4%) were diagnosed with TB. Mean age of index and HHCs were 36.6 ± 13.2 and 23.3 ± 14 years respectively. HHCs were followed-up for an average 2.1 ± 1.1 years (range 1-5 years). 75 (4.4 %) HHCs developed TB during 4094 person-year follow-up with an incidence of 1.8 per 100 person-years (95%CI : 1.4-2.2). HHCs had eight

times (RR: 8.18; 95%CI : 6.3-10.6) higher risk of developing TB compared to the estimated TB incidence among general population of 207/100 000. More than half (39/75) of new cases were diagnosed within the first year of the index case diagnosis (OR:17.9, 95%CI :9.2-34.8) and the majority (64/75) occurred among adults (OR:4.2; 95%CI : 2.0-8.8).

Conclusions: Examination of HHCs of TB cases enable diagnosis of additional cases with active TB.

PD-1167-29 Provider behavior change in the private sector: model to improve TB diagnosis

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Background: India accounts for 27% of the global TB notifications and one-third of the estimated annual 3 million missed cases. Nearly 50% of TB cases are treated in an unregulated private sector that is characterized by low utilization of sputum smears, low availability of quality-assured tests, large markets for unreliable serological tests, and market incentives that add to patient costs. Engagement of the private sector is critical to increase case notifications and improve TB diagnosis and treatment.

Intervention: We implemented a Private Provider Interface Agency (PPIA) model in Patna district, Bihar that engages private allopathic providers to facilitate free, quality TB diagnostic and treatment services through e-vouchers; and notify TB cases to Government of India. Patient diagnostic and prescription data was analyzed to identify provider-level behavioral trends across key metrics of notifications, microbiological testing and confirmation of TB, and drug susceptibility testing with Xpert MTB/RIF. 'Poor-performing' providers were targeted by field teams with increased frequency of communication, one-on-one sensitizations on Standards of TB Care (STC), and sharing of newer program initiatives.

Results: Between 3Q 2014 and 4Q 2015 PPIA achieved 42% provider coverage with 658 providers engaged and 426 active providers notifying a total of 15,096 pulmonary TB cases. Case notification rate nearly quadrupled from 95 to 363 by 4Q 2015 after initiation of PPIA. Among PPIA notified cases, microbiological testing (via smear microscopy or Xpert) improved from 19% to 29% with Xpert testing improving from 13% to 30%. Microbiological confirmation increased from 12% to 20% with positivity improving from 37% to 50% (Figure 1)

Conclusion: PPIA implementation in Patna suggests that it is possible to engage private providers to drive behavior change. Data utilization and data sharing

around key metrics and subsequent targeting of providers has potential to individually and collectively improve notification rates and TB diagnosis.

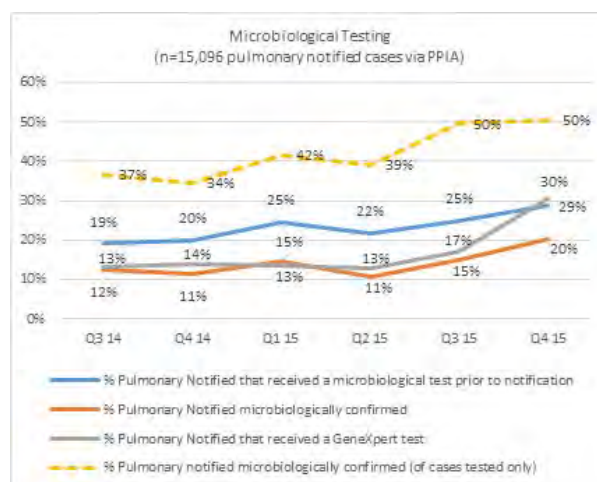


Figure Microbiological testing

PD-1168-29 Contributions of faith-based organizations in improving TB-HIV testing in Indonesia

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Background: The 2013/14 Indonesian national TB prevalence survey gave an unexpectedly high prevalence of 1.6 million cases, giving Indonesia the world's second largest TB burden, measured by prevalence, behind India. The WHO classifies Indonesia as a high TB and high TB/ HIV burden priority country. Although TB-HIV collaborative activities (TBCA) began in Indonesia in 2007, only 2.9% of TB patients in 2014 were with known HIV status. Furthermore, Provider Initiated Testing and Counselling (PITC) is not implemented widely yet. The program covering 12 provinces and 48 districts.

Intervention: Cadres and religious leaders were recruited and trained to screen for symptoms of TB. The Religious Leaders were socializing TB-HIV among their jamaa' (recitation followers) at houses or mosques. Individuals suspected of having TB were then referred to a health facility for smear microscopy. Cadres facilitated transportation to ensure testing occurred. When a patient was detected, the cadres with the help of health officers initiate to HIV test and follow up TB treatment. In addition, cadres are given a reward for case finding, case holding and HIV testing.

Results: Recruiting religious leaders and cadres within 'Aisyiyah structure has helped to improve TB Case Finding. Nationally, Aisyiyah asked to contrib-

ute 7% of the national target. In January-June 2014, 'Aisyyiah were able to contribute 10% of the target and the number has gone up to 14% in the same quarter for the following year. The religious leaders were provided by IEC Material on TB-HIV in Islamic context. The cadres are motivated to seek TB Patients and accompany them for treatment, this was told as part of worship. Related to HIV Test, in January-June 2015, 21% of TB Patients were having an HIV Test and know their status (1120/5329 TB Patients), this is higher than the setup target by 15%.

Conclusions: This approach demonstrates that involving Faith-Based Organization (cadres and religious leaders) can be a highly effective solution for improving case finding and HIV test. Further effort is required to study the TB treatment adherence as the 90% national target was not achieved yet.

PD-1169-29 Factors influencing sputum smear conversion after two months of tuberculosis treatment in Addis Ababa, Ethiopia

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Introduction: Sputum smear conversion is the most important indicator in evaluating the effectiveness of treatment and the infectivity of the disease. But little is known about factors associated with delay in sputum smear conversion at the end of 2nd months of treatment in Addis Ababa.

Objective: To identify factors influencing sputum smear conversion at the end of 2nd months of treatment in new smear positive adults treated in AA public health centers.

Method: Case-control study was performed in Addis Ababa public health centers from December 6/2012-January30/2013. Cases were 78 sputum smear positive TB patients who started anti-TB from the period of February 9 to October 10/2012, with positive sputum smear at the end of second months of anti-TB, randomly selected from the prepared sampling frame. Controls, two for each case were recruited from the same health facility and nearest date of diagnosis to each case with negative sputum smear at the end of second months of anti- TB treatment. Data were collected using a pre-tested questionnaire by trained data collectors. Data was entered into a computer using EPI-Info version 3.5.1 and analyzed using SPSS version 20. OR & 95%CI used to measure the associations.

Results: After adjustment for potential confounders, male (OR=2.13; 95%CI 1.11-4.08, P=0.023), current smoker (OR=3.38; 95%CI 1.25-9.14, P=0.017), Absence of BCG scar (OR=2.54; 95%CI 1.33-4.88, P=0.005), low BMI (< 17kg/m²) (OR=4.61; 95%CI 2.04-10.38, P< 0.001), HIV positivity (OR=2.64; 95%CI 1.28-5.46, P=0.009) were independently

associated with non-conversion of sputum smears at the end of second months of treatment.

Conclusion and recommendations: Sputum smear conversion appears to be related to patients' BCG vaccinations, BMI, HIV status, sex and smoking. Health education with emphasis on dietary advice and quitting smoking should be given to all patients. Closer follow up of patients with the above risk factors and further studies with larger sample size should be important.

PD-1170-29 Dose anti-tuberculosis treatment increase the risk of biliary events?

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Background: Tuberculosis (TB) remains one of the most important infectious diseases worldwide. Adverse reactions are not uncommon while treating TB patients. However, there was little report on treatment-related biliary event (BE), such as cholelithiasis, biliary obstruction, acute cholecystitis, and cholangitis.

Methods: We conducted a nationwide cohort study using the National Health Insurance Research Database (NHIRD) of Taiwan. We identified TB patients from 1996 to 2010 and compare the risk of BE in the initial 180 days of treatment with their age- and gender-matched controls. Risk factors of developing BE in pulmonary TB patients were identified using logistic regression analysis.

Results: From the NHIRD, a total of 163 119 TB cases were identified from 1996 to 2010. Among them, 195 developed BE within the initial 180 days of treatment. TB patients had a significantly higher BE risk than their matched controls (0.11%). Independent risk factors of BE were age (RR, 1.03, 95%CI 1.02-1.04) and diabetes mellitus (RR 1.59, 95%CI 1.19-2.13).

Conclusions: Anti-TB treatment may increase BE risk. Though not frequently encountered, acute BE should be considered in TB patients who suffered from abdominal discomfort with hyperbilirubinemia, especially in old age and diabetic patients.

57. Tobacco dependence and cessation

PD-1171-29 Tobacco and marijuana use in young men presenting for medical circumcision in South Africa

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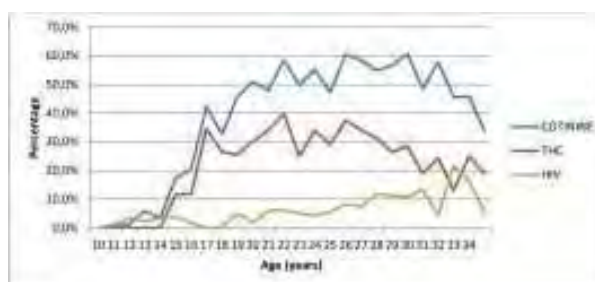
Background: Most recent estimates in South Africa report that 21% of people have a history of tobacco smoking, with men (32%) having thrice the prevalence of women, and intensity increasing with age. There is limited recent data on tobacco and tetrahydrocannabinol (THC) use in young South Africans. Voluntary medical male circumcision (VMMC) to prevent HIV acquisition offers opportunity to rapidly survey large numbers of young men.

Methods: We report interim results of a current cross-sectional study among men (10-34 years) attending five VMMC clinics in South Africa. After consenting, participants are interviewed and provide a urine sample for cotinine and THC testing. Cotinine positive participants are breathalyser-tested for carbon monoxide in parts per million (COPPM). Following manufacturer guidelines COPPM scores are categorised as: mild, moderate and severe. Participant HIV status is recorded.

Results: Among 1377 participants, 440 (32%) were self-reported current smokers of whom cotinine was positive in 91.8% (403/440); 22.8% (13/57) of self-reported past-smokers and 4.9% (42/854) of self-reported non-smokers were also cotinine positive. Severe smoking was found in 51.5% of those testing cotinine positive, of whom 97.8% (223/228) were self-reported current smokers. Severe smoking was observed >14 years. Urine THC was positive in 18.8% of these 54% self-reported using both. Half the marijuana users were 19-25 years. Overall HIV prevalence was 5.4%. Cotinine positivity in HIV-infected men was significantly higher than in HIV-seronegative men (46.6% vs 32.7; $P=0.01468$). Tobacco and marijuana use showed a parabolic increase with age (Figure).

Conclusion: In this cross-sectional survey, >50% of young men requesting circumcision were cotinine positive by 19 years with a rapid increase in prevalence of both cotinine and THC from age 14. Innovative evidence-based and age-targeted interventions, to prevent initiation and encourage cessation, and to reduce escalation, of both tobacco and marijuana use should be implemented in VMMC clinics.

Figure Prevalence of cotinine, THC and HIV by age group



PD-1172-29 Exploring the role of black cumin seeds (*Nigella sativa*) in overcoming nicotine dependence

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Background: Nicotine is one of the most addictive substances known to humanity. Nearly 80% of the world's 1 billion smokers live in low and middle income countries most of which do not have enough resources to sustain a tobacco-cessation program at the community level. Apart from smoking, use of chewable tobacco is a big problem in high burden countries like India, Bangladesh, Pakistan. Rampant use of cheaply available gutkha has made cancer-victims of young persons, many in their early 20s even. Tobacco-chewers are also habituated to the act of chewing. A mix made of 20% black cumin seeds was prepared and administered to the test group. In recent studies black cumin has been found to be beneficial in opioid dependence. This is based on its ability to block calcium channels, an activity which has also been identified in nicotine dependence.

Methods: 80 heavy tobacco-chewers with a Fagerstrom Score of more than 5 who volunteered for the study were divided into study and control groups of 40 subjects each. The test group was provided with the mix containing 20% black-seeds with fennel while the control group was given the mix comprising of fennel and bishop's weed both of which are commonly consumed condiments. Subjects were advised to take the mix twice daily, first dose after the breakfast and then again after supper. After 1 week of treatment their Fagerstrom Scores were taken and then again every week till the end of fourth week.

Results: Subjects in the study group reported an average improvement of 3 points in their Fagerstrom Score ($P < 0.001$) while there was an average improvement of 1 point in the control group. Subjects

in the study group were also more motivated to quit tobacco-chewing.

Conclusions: Black cumin seeds can be used as a potent quitting substitute especially in tobacco-chewers and more so in communities where black-seeds are considered auspicious (e.g. Muslims). Also it has been scientifically established that black-seeds is effective in blood pressure control, lowering blood cholesterol and it also has anti-neoplastic properties. The anti-addictive properties of black cumin looks promising and merits further exploration.

PD-1173-29 Heaviness of smoking index, cigarettes per day, and time to first smoke in settings of multiple tobacco products use

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Background: Cigarette smoked per day (CPD) and time to first smoke (TTFS) are standalone indicators of nicotine dependence as well as used as heaviness of smoking index (HSI) in combination to assess dependency level quickly. TTFS is considered as more reliable than CPD for assessment of nicotine dependence. Lower consumption of cigarette in South East Asia countries due to various socio-economic-cultural influences, and simultaneous usage of multiple forms of tobacco products remains a threat to validity and reliability of CPD, TTFS and HSI in assessing nicotine dependence. This study is aimed at assessing the usefulness of these indicators in explaining dependence outcome measures.

Methods: GATS-India data were analyzed considering daily consumption of manufactured cigarette and the consumption was classified as exclusive cigarette user and multiple user of tobacco products. CPD, TTFS and HSI were compared with dependence outcome indicators like past quit attempt in the past year and future quit intention. As a non-random sub-sample was issued to analyze dependence outcomes within individuals, GATS weight was not used.

Results: In exclusive cigarette-only use setting low CPD (≤ 10 sticks) explained 90.4% of quit attempt ($P=0.537$) and 92.7% of positive quit intention ($P=0.004$). While TTFS ≥ 30 minutes explained 56.4% of quit attempt ($P < 0.001$) and 51.3% of positive quit intention ($P=0.029$). HSI score ≥ 4 explained 3.5% of no quit attempt ($P=0.124$) and 4.5% of no quit intention ($P=0.029$). Similar trend for CPD and HSI were observed in multiple use settings. But TTFS ≥ 30 minutes explained only 45.4% of quit attempt and 41.1% of no-attempt ($P=0.001$), as well as 55.2% of quit intention and 61.3% of no intention ($P < 0.001$).

Conclusions: Thus TTFS performed better than CPD and HSI to explain the dependence outcomes in cigarette-only use settings but failed in the multiple

use settings. Mixed consumption of multiple tobacco product affects nicotine intake and hence cigarette consumption as well as TTFS. Therefore, in multiple use settings time to first tobacco to assess nicotine dependence quickly need to be explored.

PD-1174-29 Preparedness among health professionals for tobacco cessation and control in South India: an exploratory study

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Background: Smoking is the one of the most preventable causes of death worldwide. Oral health professionals may play an important role in anti-smoking campaigns. The aim of this study was to evaluate current knowledge of and attitudes toward smoking and preparedness for cessation among dental professionals. The 5As approach is a clinic-based approach and has been developed for health care providers who are uniquely positioned to interact with tobacco users.

Methods: The study was a cross-sectional study conducted among 498 dental health professionals (dentists) in the state Karnataka, South India. Descriptive analysis and chi-square test were employed to test the differences in knowledge levels and practices of dentists. Bivariate logistic regression was used to examine the association between each predictor variable separately and the outcome variables after adjusting for age and location. Data was analyzed using SPSS version 21 software.

Results: Majority of dentists reported that they were aware of respiratory illnesses, tuberculosis, lung and oral cancer as conditions caused due to tobacco consumption. Awareness of adverse reproductive and child health effects associated with tobacco use was very low. Few respondents informed all patients about harmful effects. Almost all the dentists had received a formal theoretical knowledge about tobacco cessation but only 22% of dentists reported having ever received any on-job training related to tobacco control. Dentists who reported receiving training in tobacco control were more likely to provide information on health effects of tobacco as compared to those who reported not being trained in tobacco control in the state of Karnataka.

Conclusions: A majority of Oral health care providers ask patients about tobacco use but provide advice only to patients suffering from specific diseases. A context-specific capacity building package needs to be designed to equip dentists in recommended 5As approach in tobacco cessation. More meaningful participation of dental professionals in tobacco cessation is needed, with implications for related curriculum changes.

PD-1175-29 Estimation of salivary thiocyanate levels among tobacco users, passive smokers and tobacco non-users: implications in tobacco cessation

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Background: The Global Adult Tobacco Survey - India 2010 reports that about 275 million adults consume tobacco of which 206 million use the smokeless form. Thiocyanate (SCN) present in the body fluids is partially because of detoxification of hydrogen cyanide in smokers. About 3-fold higher concentrations of thiocyanate are found in sera, urine and saliva of smokers as compared with non-smokers. Although studies have shown that salivary thiocyanate is a suitable indicator of habitual smoking, data on its levels among tobacco chewers is lacking. Hence, the present study aimed to estimate and compare the salivary thiocyanate levels among smokers, passive smokers, tobacco chewers, non-tobacco users.

Methods: A hospital based observational study was conducted on 100 patients. Based on the responses obtained from a self-administered, pretested questionnaire, the subjects were categorized into Smokers (25), Non-Tobacco Users (25), Passive smokers (25) and Smokeless tobacco users (25). Saliva was collected from the subjects in sterile plastic containers and sent for biochemical analysis for estimation of salivary thiocyanate levels. The results obtained were tabulated in Microsoft Excel for Windows and subjected to statistical analysis using SPSS statistical package 17.0. Kruskal Wallis test was used to compare the data among the various groups and the difference was considered as statistically significant if $P < 0.05$. Pairwise comparison between groups was done using the Mann Whitney U test.

Results: The results of the present study showed that the mean salivary thiocyanate levels among the smokers was 79.46 ± 7.80 mMol/L, non-tobacco users was 36.61 ± 5.84 mMol/L, passive smokers was 50.59 ± 6.87 mMol/L and smokeless tobacco users was 50.16 ± 13.83 mMol/L. The salivary thiocyanate levels were statistically significant among various groups. Pairwise comparison of the groups showed there was no significant statistical difference between the passive smokers and smokeless tobacco users although all the other pairs showed significant difference.

Conclusions: The study concluded that salivary thiocyanate can be used as a reliable diagnostic marker for differentiation of tobacco users from non-tobacco users. Salivary thiocyanate levels may also be a simple and valuable indicator in tobacco cessation

clinics for assessing the prognosis of tobacco abusers in their attempt to quit the habit.

PD-1176-29 Smoking cessation advice from midwives during the perinatal period in Greece

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Background: Active and passive smoking during the perinatal period is undoubtedly one of the most important preventable causes of a variety of unfavorable pregnancy outcomes. Despite being informed about the risks at least one third of women still smoke during pregnancy. Greece has a smoking prevalence of 38%. It is essential for midwives to be trained in smoking cessation in order to help pregnant effectively to quit. Most women who quit smoking during pregnancy without following a smoking cessation program usually resume smoking within 6 months after delivery.

Methods: We surveyed 294 midwives in Athens (professionals & students) in 2015 using a questionnaire to ascertain their perception and knowledge on: 1) the risks of active and passive smoking in pregnancy, 2) smoking cessation in general, 3) smoking cessation as part of their duty and 4) the kind of information and help they should provide to pregnant smokers.

Results:

1. Almost all participants reported that they routinely inform pregnant smokers about the risks of active and passive smoking.
2. The vast majority (97%) believe that smoking cessation is an important part of their role.
3. Only 51.7% reported feeling comfortable in offering quitting support.
4. 87.4% reported that pregnant women were not well informed about the risks of active and passive smoking.
5. Both professional and student midwives have insufficient knowledge on the effects of smoking during pregnancy and lactation (only 1% answered correctly all relevant questions).

Conclusions: We conclude that midwives want to help pregnant smokers to quit. They should efficiently advise pregnant and breastfeeding smokers to quit. In order to be effective in this role they should be adequately educated on the actual effects of smoking during pregnancy and lactation and trained in smoking cessation strategies.

PD-1177-29 National Tobacco Cessation Programme, Sri Lanka

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Background: In Sri Lanka, the highest percentage of non-communicable disease deaths is due to tobacco usage. The highest number of tobacco related deaths is lung cancer. In having identified this problem, Foundation for Innovative Social Development (FISD) initiated a programme in five districts at community level.

Intervention: The 'National Tobacco Cessation Programme' was designed with the aim of creating awareness on the importance of terminating tobacco use through the promotion of a community based hotline which individuals are able to contact for help and in establishing a community concentrated mechanism to aid users to quit. Promotions targeting users and families were conducted via local organizations, community networks and media through the distribution of leaflets, posters, videos, handbills and stickers. The programme consists of four stages which users are encouraged to undertake; information dissemination, where individuals are given to read and understand; training/ workshop, conducted for the tobacco users to reduce their use and educate them on the real harm of tobacco use; counseling, is made available with professional counselors; and medical treatment is undertaken in the final stage with FISD playing a key role in rehabilitating users. A hotline each for the five districts was set up for community members to contact in regard to undertaking the programme or seeking advice on the cessation of tobacco use. A rehabilitation center was constructed by FISD which is utilized by trained doctors and professional counsellors engaged with FISD. If participants are unable to follow through with the process, they are guided back to the initial stage where they are then able to undertake a one, two or three day workshop, depending on the user's situation and educational background.

Results: The programme was undertaken by 5350 individuals. With the initial success of the programme at community level, a national level hotline '0112 887 666' was established. With 1754 individuals undergoing positive change, only 87 individuals relapsed during the various stages.

Conclusion: As such, the results and inputs received regarding this programme through participatory individuals and community members indicate that it is possible to influence discontinuing tobacco use.

PD-1178-29 Effects of mass media tobacco control campaigns in Indonesia

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Background: Indonesia is the fifth largest tobacco market in the world. It was estimated that tobacco consumption caused the death of 300,000 Indonesians per year. Mass media campaigns are a core and proven intervention for tobacco control. Given this background, Vital Strategies conducted anti-tobacco campaigns in Indonesia in May and October 2015.

Methods: A post campaign survey was conducted to evaluate the recall and impact of the anti-tobacco campaigns in Indonesia. The objective of the paper is to measure the impact of campaigns in terms of knowledge, attitudes, and practice around smoking and second hand smoking (SHS). Systematic random sampling was applied for sample selection. Total of 1500 respondents were surveyed. Chi square test and regression analysis is done to measure the impact of campaign.

Results: Approximately three-fourth of the respondents have recalled the campaigns. Both the campaigns were found to have communicated effectively, with a majority of respondents who recalled seeing the **advertisement reported** that it was easy to understand, made them stop and think, personally relevant to them, provided new information, and made them feel concerned about smoking.

Smoking habit was found less and attempt to quit smoking are higher among aware group than unaware group. Smokers who are aware of campaign are more likely to stop smoking in public places than those who are unaware of the campaigns. Awareness of campaign has increased knowledge and has made people to start discuss harms of smoking and SHS. It also reveals that those who are aware of campaigns are more likely to have changed attitude towards smoking and SHS as compared to unaware. Additionally, campaigns have also created public support for government implemented tobacco control campaigns and activities.

Conclusions: The messages the campaign advertising sought to convey were remembered and taken on board as new learning by smokers to the extent that attitudes to smoking and SHS changed. Overall, these effects applied to males and females, older and younger participants and smokers and recent quitters at all levels of educational attainment and occupational status.

PD-1179-29 Smoking cessation process

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Introduction: Serbia has ratified the Law on protection from exposure to tobacco smoke. The Law regulates all working and public places to be a smoke-free.

Objective: Consideration of the effects of smoking cessation by gender, education and the employment status in 2010 when the Law is ratified.

Methodology: We analyzed the results of patients who came to the counseling for smoking cessation from 2010 to 2015. Results of the 5-year analysis were processed by descriptive method and using T-test for two dependant samples. Successfulness was confirmed by measuring of CO in the exhaled air.

Results: A total of 2,030 smokers were interested for the smoking cessation program in the our counseling from 2010 to 2015. Of these, 1,489 smokers attended the program, and 1,134 (75.7%) finished it. The Law motivated 187 (16.5%) smokers to participate in the cessation program. There were 34.6% men (M) and 65.4% women (W). The majority of subjects (59.9%) had the secondary school education 59.9%. There were 64.7% employed smokers in total. Out of the total of 1,134 smokers, 37.7% successfully quit, 32.6% had a relapse and the remaining 29.6% subjects did not stop with smoking. Regarding the gender, women (40.4%) were more successful than men (32.7%). Women with the secondary school and those not employed (60.7%, 30.7% respectively) were significantly more successful than men (43.7%, 21.9% respectively) ($P < 0.01$). Men with higher education and male students (54.7%, 7.8% respectively) were significantly more successful than higher education and female students (36.0%, 1.3% respectively) ($P < 0.001$). In regards to the number of relapses, there were no significant differences, although non-employed men had a relapse more often (31.5%) than non-employed women (24.1%). Among the subjects that did not stop with smoking there were no significant differences in regards to the gender, education and the employment status.

Conclusion: The biggest number of employed subjects who attended the smoking cessation program can be associated with the ratification of the Law that regulates the working places without the tobacco smoke. On that way the Law initiated the initiative among the employed persons for the smoking cessation.

PD-1180-29 Readiness to quit addiction: a study among patients attending a tertiary care hospital in Western India

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Background: Tobacco use has been an important public health problem in India. Tobacco cessation is considered a cost effective intervention in controlling the tobacco epidemic in terms of preventable morbidity and mortality. Readiness to quit is one of the key steps in the process towards tobacco cessation. However, it is important to know the addiction pattern in the particular region so as to initiate de-addiction initiatives. So the current study was carried out with an objective to find the addiction habits and readiness to quit addiction among patients visiting GMERS Gotri General Hospital, a tertiary care hospital attached to Medical College in Gujarat, India.

Methods: All the patients at the registration desk of the hospital were randomly selected during May 2015. A total of 626 patients having any form of addiction were enrolled in this cross sectional study after taking written informed consent. They were interviewed in vernacular language using a validated semi-structured questionnaire. After counseling them for quitting tobacco use, their readiness to quit was enquired and those willing were referred to de-addiction clinic in Psychiatry department. Data was entered and analysed using Epi Info Software.

Results: Out of 626 addictive patients registered, 97% were males, 50.8% in the middle age group and 59.3% from rural areas. The most common form of addiction was tobacco chewing (66.4%) followed by smoking (32.7%) and alcohol (19.4%). Among them 428 (68.4%) showed readiness to quit. Out of those ready to quit 198 (46.2%) were actually registered at the de-addiction clinic.

Conclusions: Majority of patients were ready to quit addiction, so there is a need to have an ongoing program for awareness among patients about the de-addiction services already available within the hospital to improve quit rate. An awareness kiosk at the outpatient department can be explored in further studies.



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