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ABSTRACT BOOK

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PERSPECTIVES ON GLOBAL AND NATIONAL ADVOCACY TO REACH STOP TB TARGETS

MDR-TB-HIV work of MSF in Khayelitsha, including community-based treatment

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Access to treatment of drug resistant tuberculosis (DR-TB) is limited in most high TB burden settings, with most existing programmes treating small numbers of patients in 'pilot' programmes. Additionally, there are few programmes providing treatment for DR-TB in high HIV prevalence settings. In Khayelitsha, South Africa, treatment for DR-TB is provided through primary care clinics and is integrated with both the routine drug-susceptible TB programme and with the provision of antiretroviral treatment for HIV. This model of care provides a basis by which DR-TB treatment can be scaled up in high HIV prevalence settings.

Qualitative tracing of rifampicin: understanding pharmaceutical market forces

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Aim: To understand the market and other forces driving the distribution and sales of TB drugs in India and Nepal.
Design and methods: Mapping the patterns of production, distribution, marketing and retail of rifampicin and associated TB drugs in three regions of South Asia (Nepal, West Bengal and Uttar Pradesh) through qualitative semi-structured interviews with producers, medical representatives, pharmacists (including distributors and retailers), service providers (qualified and unqualified), and TB programme managers, donor agencies and activists. Over 80% of the interviews were recorded and transcribed, and where necessary translated. Unrecorded interviews and observations of interactions were noted down at the time and later typed up.
Results: Patterns of availability of TB drugs in India and Nepal differ. Nepal is dependent on imports and fixed dose combinations (FDCs) are increasingly available on the market from reputable Indian companies. Reported decreased sales of TB drugs from private retailers are associated with the success of the NTP's DOTS programme. In India, where up to 75% of TB drugs sales are outside of the public sector, there are more combinations available from a greater number of companies. FDCs are increasingly promoted by the bigger companies following the WHO advocating their use, but companies also respond to private prescriber patterns. Different regimens and combinations are marketed by companies based on how they differ from other brands. The DOTS programme in the areas researched in India seems to have had less impact on the availability of TB drugs than in Nepal.
Conclusion: It is possible to understand the patterns of availability of TB drugs in the private market through qualitative research amongst those responsible for their production, marketing and distribution. Understanding these perceptions is important for planning of service provision, and how to develop partnerships with the private sector.

Stigma and TB: comparative qualitative research across three countries

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Background: As part of a multi-country study investigating the causes of TB-related stigma in Bangladesh, Nepal and Pakistan, the relationship between stigma and precautions against TB transmission was explored.
Methods: Qualitative interviews (75) with TB patients, their family members and health workers and focus group discussions (7) with TB patients and community members were conducted and analysed using the approach to grounded theory.
Results: This study found that self-protective behaviours arising from a fear of TB transmission (such as physically distancing oneself and separating eating utensils) are both seen as natural and justified and, paradoxically, as signs of hatred towards a TB patient. This is because precautions against TB transmission (reduced proximity and increased separation) are in direct opposition to caring behaviours. This leaves families and friends with a dilemma: to demonstrably care for a TB patient or to protect themselves. Whether behaviours are interpreted as precautionary or as uncaring (and therefore hateful) depends on the emotional state of the patient, what precautionary behaviours are deemed to be legitimate, who initiates the precautionary behaviours, towards whom and in what circumstances, and how noticeable the behaviours even are.
Conclusion & recommendations: Increasing the knowledge that TB is transmissible and increasing perceptions of risk are likely to exacerbate the fear of TB, and therefore the fear of people with TB.

Reducing fear by reducing actual and perceived vulnerability to TB and its consequences is likely to reduce stigma. Furthermore, increasing clarity and consistency (especially for TB patients) on what constitute necessary precautions and promoting those which are feasible and socially appropriate, and can therefore be interpreted positively as caring, is important for both reducing TB-related stigma and increasing TB control.

Experiencing MDR-TB in Nepal: orienting programmatic responses to be more patient-centred

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Background: Multi Drug Resistance (MDR) rates among new and former TB cases in Nepal are 2.9% and 11.7% respectively. The Nepal National Tuberculosis Programme (NTP) started treating MDR TB in September 2005 using standardized treatment regimens. People with MDR TB require directly observed treatment for a minimum of 24 months, which means they need to be near to the treatment centre. At the outset, the programme did not provide social or financial support.
Objective: To understand social and financial issues affecting continuation of MDR TB treatment and help the programme to design ways of providing socioeconomic support appropriate to the context and needs of people with MDR TB.
Methods: Qualitative research using in-depth interviews with people with MDR TB, their families and service providers.
Results: Access to MDR treatment was a problem especially for people living far from a treatment centre. Subsequently, completing the lengthy (24-month) regimen was extremely problematic especially for poor who had already experienced a long and complex history of TB/MDR TB diagnosis and treatment. Suffering was greatly exacerbated by high costs, despite provision of free drugs in the programme, arose from essential relocation to accommodation nearby the treatment centre: these costs were unmanageable. In addition, many people required social support, since relocation removed them from their normal support networks (family and friends): but no provision was available.
Conclusion: The study result contributed to policy development. The NTP started to provide financial support to people with MDR TB during treatment. This is an important step towards patient-centred MDR TB services; however, this financial support needs to be extended to cover other costs such as living costs. There is a need to identify an appropriate social support mechanism to address social issues faced by people with MDR TB.

Integrating individual stories with policy: the role of qualitative methods

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How deep do qualitative methods go and how much are they valued in TB control policy and strategy? How much do stories tell us about populations? In international TB policy, the emphasis and power of perspective is currently held by 'numbers', but what of qualitative accounts and methods, how important are multi, trans and interdisciplinary perspectives in TB control? What can we learn from a story of a person with TB that provides us with enough information to manage, prioritise and direct our TB programme? This presentation will call on individual stories of people with TB to answer these questions. TB policy requires a balanced, and 'wholesome approach' to how it directs staff and patients and this can be provided through a greater emphasis and awareness of the power of qualitative methodology and methods.

Beyond 'study subjects': community members' insights into the design of TB clinical trials

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Setting: Manhiça District, Maputo Province.
Objective: To explore health seeking behavior for TB outside the formal health system and to identify TB care givers in the community in preparation for TB vaccine trials.
Design: 7 Focus group discussions (FGD) with community members and 20 interviews were conducted with traditional healers and informal medicine sellers.
Results: All of those consulted tended to think that TB does not exist in children, even when a specific child presents with symptoms of TB. The majority of informal providers in the community consider that TB symptoms are a consequence of adults' transgressive or contaminating sexual practices. By contrast, most FGD participants tended to trace the origins of TB to migratory work in the South African gold and diamond mines. In fact throughout southern Mozambique, popular narratives suggest that men returning from migrant labor suffer from TB due to adverse conditions encountered in the mines. The FGD high-

light community members' confidence in the ability of informal providers to cure TB. No community member reported having acquired medication from informal vendors. By contrast the informal sale of medicines was criticized and discouraged by almost all participants.

Conclusions: The early detection and treatment of TB in infants, children, and adults will require enhanced community awareness and outreach efforts. The district TB program should work closely with traditional healers to reach patients.

Perceptions of study procedures in TB vaccine trials involving children in Luo

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Aim: To learn the needs and expectations of communities to prepare for future TB vaccine trials.

Design: 27 focus groups (FGD) were conducted with 244 parents and traditional birth attendants in Luo communities in Siaya District, Nyanza Province in Western Kenya.

Methods: Discussions were conducted in Dholuo and were audio recorded and transcribed verbatim. Luo Social Scientists and note takers used a topic guide to facilitate the FGD, which covered: acute illness care seeking attitudes and behaviours, perceptions of study procedures in TB investigation (gastric aspiration, chest radiography, verbal autopsy), as well as recruitment, retention, and vaccination practices used in vaccine trials. The transcripts were imported into NVivo 8 for thematic analysis.

Results: Participation in clinical research is seen by some as a means to access scarce health care resources, health education, transport, or treatment. In general, research was felt to bring both immediate and future benefit to their community and their children and was often associated with modernity and 'development'. Parents' decision-making criteria for infant trial involvement include an assessment of who the researchers are, how they relate within the village, and how well procedures, risks, evidence of health benefit, and time demands are presented. Fathers and mothers had distinct concerns. Mothers were wary of blood draws and gastric tubes, whereas fathers tended to raise issues with overnight travel and hospitalization costs. Some were unclear about how research is authorized and key differences between testing investigational vaccines and routine immunization.

Conclusions: Communities appreciate the gravity of the TB-HIV epidemic and are willing to fight it. TB trial communication should emphasize the experimental nature of research to preclude therapeutic misconception.

A Conceptual Model to Explain TB Vaccine Trial Participation

ADVANCES IN MDR-TB TREATMENT: FINDINGS FROM RECENT OBSERVATIONAL STUDIES AND CLINICAL TRIALS

Linezolid for MDR-TB treatment: the LiMiT study

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Setting: Patients with microbiologically confirmed M(X)DR-TB admitted to a specialist TB hospital in Durban, South Africa.

Objectives: Available treatment regimens for M(X)DR-TB are limited by insufficient potency, side effects, long duration, expensive and limited experience in HIV co-infected patients. Linezolid is increasingly being used off-label for M(X)DR-TB. We conducted a pilot study to evaluate safety, tolerability and efficacy of linezolid in M(X)DR-TB.

Design: Patients were enrolled in a randomized, double-blind pilot study of low-dose 600 mg daily, linezolid plus optimized background therapy (OBT), for 16 weeks. OBT included >4 anti-TB drugs based on susceptibility results. Treatment was directly observed 7 days per week. Patients had fortnightly

clinical, laboratory and mycobacteriologic follow-up for 16 weeks.

Results: 389 patients were screened for enrolment. Of 36 patients enrolled, 24 (66%) were HIV infected and 24 completed study therapy. The median age was 34 years. The mean CD4 count at baseline for those HIV infected was 259. Eleven patients withdrew from the study; 8 withdrew before completing week 3 of study therapy, and none provided a reason for withdrawal. Study follow-up is near completion. To date, there have been 2 serious adverse events unrelated to study drug, and no significant hematologic toxicities. There were 15 grade 1–2 peripheral neuropathies, of which 10 have completely resolved.

Conclusions: Many patients needed to be screened to identify eligible participants. The early dropout rate was high. Of the 14 patients that were evaluable for efficacy, there were no safety concerns associated with study therapy.

TMC-207 versus placebo plus OBT for the treatment of MDR-TB: a prospective clinical trial

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TMC207 is the first in a new class (diarylquinoline) of anti-tuberculosis (TB) drugs to inhibit mycobacterial ATP synthase. It is a promising agent to improve treatment of both drug-sensitive (DS) and multidrug-resistant (MDR) TB. It has potent late bactericidal properties in the established murine TB model. Six (6) phase one trials have been conducted in healthy volunteers ($n = 173$, TMC207 $n = 144$) and one phase IIa 7-day extended early bactericidal activity (eEBA) trial in patients with pulmonary TB ($n = 75$, TMC207 $n = 45$). The Phase II trial, C208, is a 2-stage randomized, double-blind, placebo-controlled trial in patients with newly diagnosed MDR-TB, comparing TMC 207 to placebo administered on top of a 5-drug standardized backbone regimen, including kanamycin/amikacin, ofloxacin, pyrazinamide, cycloserine and ethionamide. In Stage 1, 47 patients received 8 weeks of study drug (24 placebo, 23 TMC207) added to a 5-drug background regimen (BR). Patients then continued their MDR-TB treatment and all patients in Stage 1 have completed the trial. The addition of TMC207 significantly increased the proportion of culture negative subjects (48% vs. 9% at week 8) and resulted in a 58% reduction in mean time to culture conversion compared to placebo. In Stage-2, 161 patients were randomized to receive 24 weeks of either placebo or TMC207 added to the same 5-drug background regimen. All patients in Stage 2 have com-

pleted 24 weeks of TMC207/placebo plus BR and are completing 18–24 months treatment with 2nd line TB drugs. In this symposium we will present preliminary data from a planned 24-week interim analysis from Stage 2 of this trial.

Management of drug toxicity in the treatment of MDR-TB

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Background: Clinical management of multidrug resistant tuberculosis (MDR TB) requires lengthy multi-drug treatment regimens (up to two years), which usually include 4–5 toxic drugs. These drugs are often associated with high rates of adverse drug reactions and can require temporary or permanent discontinuation of causing drug or whole treatment regimen.

Objective: To analyze role of drug side effects and side effect management on MDR TB treatment.

Results: In theory in case of MDR TB more than 20 drugs (E, Z, S, Km, Am, Cm, Ofx, Lfx, Gfx, Pto, Eto, Cs, Tzd, PAS, Amox/Clv, Lzd, Clr, Th, Cfz, Imipenem) are available for treatment. In practice the number of drugs available for treatment regimen is much more less due to several reasons: 1) usually patients have resistance to more than two drugs, including also second line drugs (especially in countries with history of previous use of second line drugs); 2) drugs from one group (like injectables or FQ) cannot be used simultaneously; 3) not all drugs are available and registered in countries; 4) in many cases drugs should be excluded from regimen due to severe side effects. Experience from Latvia shows that 79% of MDR TB patients experienced at least one adverse event, with a median of three events per case. Studies from Istanbul and Tomsk showed similar results—69% and 73% respectively. Usually side effects are mild and with adequate management do not require drug discontinuation. In different studies 30–56% of cases had a causing drug permanently stopped.

Conclusion: All measures should be taken to encourage patients not to stop treatment despite all its discomforts to prevent unnecessary drug discontinuation and risk of treatment failure or development of additional drug resistance. Adequate side effects management and monitoring can prevent life threatening side effects, use of inadequate treatment regimens and development of additional drug resistance and treatment discontinuation.

BIOMARKERS FOR TUBERCULOSIS IN RELATION TO THE SPECTRUM OF HIV PREVALENCE

Gene expression profiling for biosignature definition in tuberculosis

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Biomarkers should provide accurate, consistent and objective measurements, which indicate a physiological or pathological process, or a response to a therapeutic or preventive intervention. Multiple biomarkers can be combined to a biosignature. We use gene expression profiling for biosignature definition of the host response in tuberculosis (TB). We analyze gene expression profiles in TB patients, latently infected healthy individuals, and healthy individuals not infected with *Mycobacterium tuberculosis*. We use peripheral blood leukocytes as well as selected leukocyte populations for transcriptome analysis by microarray technology. Genes of relevance are verified by RT-PCR. To correct for confounding factors bioinformatic programs are being employed. Study participants are of different origins, namely, Caucasian donors from Germany as well as donors from endemic regions in sub-Saharan Africa. Analysis of peripheral blood leukocytes from Caucasian donors revealed that three selected genes, namely, Rab33A, lactoferrin, and Fc-gamma receptor were sufficient for discrimination between latently infected healthy individuals and TB patients. Studies on cells from donors from a highly endemic area confirmed the highly discriminative power of the Fc-gamma receptor and in addition pointed to distinct innate immune-related genes as well as genes involved in apoptosis, as major distinctive factors determining the fate of *M. tuberculosis* infection. Studies with T cells from donors from a highly endemic area pointed to genes involved in immune signaling pathways, such as suppressor of cytokine signaling (SOCS), critical factors for discrimination between TB patients and latently infected healthy individuals as well as discrimination between latently infected healthy individuals and non-infected individuals. Our biomarker studies are supported by the Bill & Melinda Gates Foundation in the Grand Challenge 6 Program.

Immune biomarkers induced by BCG vaccination and *M. tuberculosis* infection

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Biomarkers capable of predicting who is at risk of developing clinical tuberculosis, and who is protected from disease, are urgently needed. Not only would such biomarkers help identify those who should receive chemoprophylaxis, but they would be invaluable in trials of new TB drugs or vaccines. Identifying biosignatures that will also work in HIV-infected individuals with reduced T cell immunity may be even more challenging. Initially it was thought that interferon-gamma (IFNg) on its own might provide a correlate of protection, but although necessary for protection, on its own IFNg does not provide a measure of protection. Therefore simple ELISAs for IFNg have been replaced by the use of multiplex assays that aim to identify biosignatures capable of predicting protection against disease, or progression to disease. The immune response induced by BCG vaccination can be used to investigate anti-mycobacterial immunity. Using multiplex assays, BCG vaccination of adolescents or infants in the UK was shown to increase many cytokines in addition to IFNg. Testing of blood samples from BCG vaccinated infants in the UK and Malawi has shown that BCG vaccination induces different immune profiles in the two settings: UK infants made greater amounts of 7 cytokines, including IFNg, in diluted whole blood cultures stimulated with PPD, but cultures from Malawian infants contained greater amounts of another 20 cytokines. Longitudinal studies are being used to assess biosignatures in both HIV negative and HIV positive subjects that, following exposure to *M. tuberculosis*, do or do not progress to clinical disease, to assess responses to TB therapy, and to help predict TB patients who may relapse following apparently successful therapy.

Biomarkers of progressive tuberculosis in a high-burden TB-endemic area with low HIV prevalence

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Setting: Karachi, Pakistan ranking 8th among 22 high TB burden countries and lowest HIV incidence. **Objective:** Identify the utility of phenotypic and genotypic biomarkers in discriminating 'putatively' protected or 'putatively' susceptible TB risk groups post acute exposure to *M. tuberculosis*. **Design:** Longitudinal assessment of biomarkers in a recently exposed healthy household cohort from single (HC = 15) or multi-case families (HHC = 35) who remain disease free or develop secondary cases (DHC = 10) during a four-year follow up period. **Results:** Cytometric Bead Array (CBA) methodology was used to determine cytokines secretion (IL2, IL4, IL6, IL10, TNFα and IFNγ: BD Biosciences) in plasma from diluted (1:10) whole blood cultures after 2 days incubation. Arm PCR was carried out for snps in IL6 (−174), IL10 (−1082), IFNγ (+874) and

TNFα (−308). HC showed significantly higher IL6 secretion compared to HHC (MWU $P < 0.0001$) in parallel with higher frequency of IL6 $\underline{G}$ high allele in HC ($P = 0.008$; $\chi = 7.11$; OR 5.2; CI 1.41–19.21). Spontaneous IL2 and IL4 secretion was significantly lower in HC compared to HHC at 0 months ($P = 0.001$; $P = 0.002$) and 6 months (IL2 $P = 0.018$; IL4 $P = 0.041$). When HHC and DHC were compared, IL4 was significantly higher in DHC at all time points (0 months; $P = 0.016$; 6 months; $P = 0.016$; 12 months; $P = 0.007$ and 24 months; $P = 0.009$). No difference in snp frequencies was seen for IL6, IL10, TNFα and IFNγ between HHC and DHC.

Conclusion: Endogenously activated IL4 provided the most discriminating marker for TB susceptibility in recently exposed household contacts of multicase families.

Biomarkers of disease severity in pulmonary and extrapulmonary tuberculosis with low HIV co-infection

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Aim: To diagnose severity within pulmonary and extrapulmonary tuberculosis in a high transmission and low-HIV prevalence region.

Design: Newly diagnosed untreated patients with pulmonary (PTB, $n = 36$) or extrapulmonary (EPTB, $n = 43$) disease were included together with healthy endemic controls (ECs, $n = 33$). PTB patients had either moderately advanced ($n = 23$) or far advanced disease ($n = 13$); while EPTB patients had either localized (L-ETB, $n = 27$) or severe disseminated forms of (D-ETB, $n = 12$) disease. All patients were HIV negative.

Methods: Whole blood cells of study subjects were stimulated with *M. tuberculosis* antigen ESAT6 and whole mycobacterial sonicate (MTBs). Supernatants were tested by ELISA to measure IFNγ, CXCL9, CCL2 and IL10 post-stimulation. Data was analyzed using the SPSS program and by the Mann-Whitney U test.

Results: In response to ESAT6 stimulation, levels of IFN-γ ($P = 0.04$), CXCL9 ($P = 0.03$) and IL-10 ($P = 0.02$) were increased in blood cells of patients as compared with those of ECs. In response to MTBs stimulation, patients showed increased IL-10 ($P < 0.001$) but decreased CCL2 ($P = 0.001$) secretion in comparison with ECs. PTB patients with moderate disease had raised MTBs- induced IFN-γ secretion as compared with those with far advanced PTB ($P = 0.014$). EPTB patients with D-ETB showed raised

MTBs-induced IFNγ as compared with L-ETB patients ($P = 0.02$), MTB-induced IL10 secretion was lowered in D-ETB ($P = 0.006$).

Conclusion: ESAT6-induced IFN-γ, CXCL9 and IL-10 can diagnose active TB in an endemic setting. MTBs-induced IFN-γ and IL-10 responses can differentiate severity of pulmonary and extrapulmonary TB. Therefore, these antigens used together could both diagnose disease and differentiate its severity.

Markers of protective and pathological antiretroviral mediated immune restoration in HIV-associated tuberculosis

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HIV-associated tuberculosis is a formidable problem especially in South Africa. South Africa has the highest incidence of tuberculosis, and the largest antiretroviral programme, in the world. This presentation will be based on the complex quadruple interaction created between two diseases and two treatments created in Cape Town, South Africa. Our studies of the immune response to tuberculosis in HIV infected people will be reviewed from the perspective of tuberculosis biology. The protective and pathological consequences of partial restoration of immunity to tuberculosis by combined antiretroviral and antitubercular therapy will also be discussed.

ALCOHOL AND DRUG USE DISORDERS, TUBERCULOSIS AND HIV: RESEARCH INTO PROGRAMME SOLUTIONS/INTERVENTIONS

Screening for alcohol use disorders among TB and HIV patients

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Background: Alcohol use disorders (AUDs) affect HIV disease by increasing the risk of transmission with unsafe sexual behaviors in people living with HIV and those uninfected, as well as impacting adherence to HIV care and management. These factors, along with alcohol's direct effect on immune system, could accelerate HIV disease progression. AUDs also affect the TB incidence and outcome by weakening the immune system leading to increased susceptibility to TB. AUDs also affect TB disease progression in settings of medication non-adherence, change in TB medication pharmacokinetics, default from TB program and poor

TB treatment outcomes. Thus, AUDs can drive these two epidemics.

Interventions: This discussion will be focused on identifying standard drinks, different screening tools for AUDs—including the CAGE, AUDIT and ASSIST. Studies that evaluate integration of screening tools in TB and HIV programs globally will be reviewed. Some of the challenges associated with effective implementation screening tool including TB/HIV provider buy-in, time constraints in TB-HIV clinical programs, cultural adaptation of tools to local settings, as well as lack of existing referral and treatment programs for AUDs, will be discussed also.

Solutions: This discussion will highlight the TB-HIV programs that have effectively integrated screening for AUDs. It will also discuss the role of a multidisciplinary team approach engaging TB-HIV patients, providers, nurses, program managers and social workers in effective implementation of integrated AUDs screening.

Screening for alcohol use disorders among TB and HIV patients

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Both heavy drinking and alcohol use disorders (AUD) have been associated with the incidence of infectious diseases including tuberculosis and sexually transmitted diseases such as HIV. Thus, screening for alcohol should include not only screening for alcohol abuse and alcohol dependence, but also questions about heavy drinking occasions. The WHO Alcohol Use Disorders Identification Test (AUDIT) contains both aspects and thus could be used as a minimal screener. If time and resources allow for addition of other measures, biomarkers for alcohol consumption and aspect of immune system damage should be considered as well as additional question on the frequency of drinking above different thresholds per occasion and/or measures for alcohol dependence. Results of the screening should be used in preparing specific interventions which could follow a stepwise plan from brief interventions to formal alcohol dependence therapy. Feasibility of embedding screening questions for AUD in routine treatment will be discussed.

Alcohol use and TB: is there a causal connection?

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Background: In 2004, tuberculosis (TB) was responsible for 2.5% of global mortality (among men 3.1%; among women 1.8%) and 2.2% of global burden of disease (men 2.7%; women 1.7%). The present work portrays accumulated evidence on the association between alcohol consumption and TB with the aim to clarify the nature of the relationship with respect to causality.

Methods: Systematic reviews of existing scientific data on the association between alcohol consumption and TB, and on studies relevant for clarification of causality were undertaken. In addition, the burden of TB attributable to alcohol use was estimated.

Results: There is a strong association between heavy alcohol use/alcohol use disorders (AUD) and TB. A meta-analysis on the risk of TB for these factors yielded a pooled relative risk of 2.94 (95%CI 1.89–4.59). Numerous studies show the pathogenic impact of alcohol on the innate and acquired immune system causing susceptibility to TB among heavy drinkers. In addition, there are potential social pathways linking AUD and TB. Heavy alcohol use strongly influences both the incidence and the outcome of the disease and was found to be linked to altered pharmacokinetics of medicines used in treatment of TB, social marginalization and drift, higher rate of re-infection, higher rate of treatment defaults and development of drug-resistant forms of TB. Based on the available data, about 10% of the TB cases globally were estimated to be attributable to alcohol.

Conclusions: The epidemiological and other evidence presented indicates that heavy alcohol use/AUD constitute a causal risk factor for incidence and re-infection of TB. Consequences for prevention and clinical interventions are discussed.

Prevalence and correlates of TB testing among persons with substance abuse disorders in Tijuana

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Objective: Over half of injection drug users and other groups at high-risk for HIV infection in Tijuana, Mexico have latent TB infection (LTBI). Since LTBI treatment can reduce the risk of reactivation by over 75%, testing and preventive treatment in high risk groups could lower the risk of TB morbidity, mortality and subsequent transmission. This study estimated the prevalence and identified correlates of tuberculin skin testing (TST) among groups at risk for HIV infection in Tijuana.

Methods: Injection drug users, non-injecting drug users, sex workers, and homeless persons ≥18 years old were recruited via street outreach to undergo a

risk assessment interview and testing for HIV and *M. tuberculosis* infection. QuantiFERON-TB® Gold In-Tube (QFT) assays were used to detect *M. tuberculosis* infection. Prior history of TST was assessed via self reports and multivariable logistic regression was used to identify correlates of TST history.

Results: Of 503 participants, 38% reported prior TST, which was associated with previous incarceration in the U.S. (adjusted odds ratio [AOR] = 13.38; 95%CI 7.37–24.33) or Mexico (AOR = 1.87; 95%CI 0.99–2.88) and injecting illegal drugs (AOR = 1.99; 95%CI 1.27–3.11). Crossing the border into the US was marginally associated with TST (AOR = 1.63; 95%CI 0.93–2.88). QFT-positivity was similar for participants with (58%) and without (56%) prior TST ($P = 0.685$).

Conclusions: Although TST was low overall, most participants who reported prior TST had been incarcerated, particularly in the US. Our findings suggest the need to increase TB screening among populations at risk for HIV in Tijuana, particularly those outside of criminal justice settings.

Integrated TB-HIV and substitution therapy services for drug users: case studies from four countries

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People who use drugs (PUD) (smoke crack or who inject drugs [PWID]) often don't receive essential health services (harm reduction, substitution therapy, TB, HIV, hepatitis services). Consequently, outcomes are poor. In 2008, WHO, UNODC and UNAIDS published guidelines on providing integrated TB-HIV and harm reduction services for PUD. A multi-country practices & experiences documentation was conducted in Brazil, India, Ukraine and Zanzibar in UR Tanzania. Qualitative methods of data collection were used involving key stakeholders, national and local policy makers, care providers and patients. Site visits of facilities were also conducted. Some service integration was identified in all countries. In Zanzibar, outreach services try to link drug users to clinical services but uptake is limited as the full package of harm reduction including opiate substitution therapy (OST) is yet to be offered. In India, organizations provide harm reduction and some OST to PWID with accompanied referrals to clinical services, including HIV and TB diagnosis, treatment and care—but barriers accessing appropriate HIV and TB treatment remain for many PWID. In Ukraine, TB, HIV and substitution therapy services are co-located at a handful of facilities but regulatory and social barriers limit scale-up. In Brazil, TB-HIV activities are rolling out nationally; federal policy affirms the right to health for PUD; but the provision of linked TB-HIV/harm reduction services targeted to PUD varies at the local level. While some integration of services is ongoing, lack of political, legislative support and sustainable funding threatens scale-up. Access to harm reduction services is a major constraint while TB and HIV co-management is often poorly understood. TB programs are rarely involved in programs targeting drug users; few countries track the burden of TB among PUD or the contribution of drug use to poor TB outcomes. Global/national advocacy to scale up these services is needed.

FAMILY-BASED APPROACH AND THE FOURTH 'I': INTEGRATING MATERNAL AND CHILD TB-HIV MANAGEMENT

Rationale for integrated approach and the challenges

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Mothers and children are at the intersection of the HIV and TB epidemics. TB is the most common HIV-related illness and cause of mortality in reproductive-aged women in Asia/Africa; HIV-infected pregnant women have a 10-fold increase in TB. Maternal TB-HIV increases postpartum mortality by 2–3 fold and infant death by 2–6 fold; infants of TB-HIV-infected mothers have higher rates of prematurity, low birth weight, intrauterine growth restriction, and possibly HIV transmission. Infants of TB-HIV-infected mothers have an increased risk of congenital/neonatal TB, regardless of the infant's HIV status. Effective TB prevention strategies must involve effective and early screening, diagnosis and treatment of TB in pregnant women at high risk. Prevention of mother to child HIV transmission programs offer an opportunity to implement such a TB screening program. The use of isoniazid preventive therapy (IPT) in pregnant women with latent TB remains controversial, but given the high risk for TB and maternal/infant mortality in HIV-TB infected women, this intervention needs study in HIV-infected pregnant women. TB is a major cause of morbidity/mortality in HIV-infected children; HIV-infected infants in South Africa had a 24-fold increased incidence of TB and 25–60% of all hospitalized children with TB are HIV-infected. Given data demonstrating 6 month IPT reduces mortality in antiretroviral-untreated HIV-infected children, the World Health Organization recommends IPT for all HIV-infected children >12 months without active TB, even in the absence of documented exposure to an active TB case. Children identified as HIV-infected in maternal-child or immunization programs, or through in-hospital testing should be screened for TB disease and receive IPT once active TB is ruled out. In regions where TB and HIV prevalence is high, integration of services related to both HIV and TB are needed to optimize

diagnosis, treatment and prevention of both diseases in women and children.

TB-HIV in adolescents: an emerging challenge

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In some Southern African cities, HIV is now the single most common cause of severe morbidity and mortality in adolescence (10 to 19 yrs), mainly due to maternally-acquired infection. It has only recently been recognised that up to one third of HIV-infected infants have slowly progressing disease, and are likely to survive to adolescence without treatment. Thus countries with very high antenatal HIV prevalence rates in the 1990s may now have 2 to 3% of all 10-year-olds being HIV-infected long-term survivors. Chronic lung disease (CLD) is the major cause of disability and death during HIV care in this age-group. This presentation will highlight insights from research in Harare, Zimbabwe, where HIV prevalence in hospitalised adolescents was 46%, of whom 20% died before discharge. Cross-sectional survey among routine HIV care attendees showed severe CLD in over 50% of adolescents. High resolution CT showed that small airways disease (obliterative bronchiolitis) considerably out-numbered cases of post-tuberculous lung disease and residual scarring from childhood lymphocytic interstitial pneumonitis. Both *M. tuberculosis* and nontuberculous mycobacteria were common opportunistic infections. Spirometry correlated well with radiological diagnosis and severity, but not CD4 count or duration of ART, implying irreversibility. Obliterative bronchiolitis can be diagnosed on histology or CT-scan, but not plain radiography. It follows viral infection (e.g. measles, adenovirus), or other small-airways insults, responds poorly to treatment, and may progress to bronchiectasis and a vicious cycle of super-infections. HIV testing practices need to be much more proactive throughout childhood and adolescence, with prompt initiation of cotrimoxazole, isoniazid preventive therapy and ART. There is urgent need for clinical trials focused on management and prevention of CLD in HIV-infected older children. Infection control also needs attention, especially screening for TB in the context of HIV.

HUMAN RIGHTS AND ETHICAL STANDARDS TO STRENGTHEN TB CARE AND CONTROL

How to deal with ethical dilemmas in practice: experience of TB programme managers

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Background: Rwanda undertook management of MDR-TB patients in July 2005 which subsequently required approbation of the GLC (Green Light Committee) for drugs purchase. To ensure standardized treatment and care along the whole country for MDR-TB patients, we developed the MDR-TB patients' management guide. The new programme received support from the Global Funds to Fight Tuberculosis, Aids and Malaria. In response to ethical concerns, the programme has introduced the rapid test since last year.

Methods: The MDR-TB management programme implemented the model of hospitalization followed by ambulatory management, among others like the strict hospitalization, ambulatory in the health facility, and community based model. We retrospectively assessed the impact of implementing this model in combination with integrating TB care and treatment ethical values.

Results: The patient's centred approach addressed the patients' rights by shortening detention during hospitalization from 6.6 months to 3.3 months between 2006 and 2009. The ambulatory phase of 14 months after hospitalization entirely covered nutritional support and transport fees of patients to health facilities. The mean reduction on time between DST results and beginning of treatment was 23 days each year from 2006 and 2009.

Other potential ethical challenges: Ethical challenges faced were at two levels: 1) challenges relating to patient's treatment which included side effects and loss to follow-up, 2) institutional challenges which include quality of TB infection control policy to protect health care workers and other categories of patients.

Conclusion: High cure rate can be achieved in MDR-TB patients' management through a patient's centered approach which promotes adherence of patients to treatment through a decentralized management in health centers nearby their home, standardized treatment regimen, management of side effects, nutritional support and transport fees coverage.

INTEGRATION OF COMPREHENSIVE SMOKEFREE POLICIES INTO HEALTH-CARE FACILITIES

Implementing tobacco-free policies and smoking cessation support in health-care facilities

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Aim: To increase awareness among health-care administrators and health professionals, that it is their responsibility to protect the health of staff and patients and their families from exposure to smoking and to help those that smoke to quit.

Method: A brief review of current best practice tobacco-free health-care policies and the provision of smoking cessation support in health-care facilities has been conducted with a focus on low- and middle-income countries. Examples of best practice models will be presented and discussed. Health-facilities need to plan well to implement an effective tobacco-free policy that will be acceptable to staff and patients and their families. They will need to establish a supportive health-care environment. This can be achieved by: conducting a campaign to raise awareness of the harm caused by smoking and encouraging quitting smoking; promoting smokefree homes; and banning the sale of tobacco products and tobacco advertising and sponsorship on the premises. Helping patients to quit, as part of a tobacco-free policy, should if at all possible be extended to helping their families to quit as well. This needs to happen in every department in the hospital, not just the respiratory and cardiology departments.

Result: Health-care administrators and health professionals should work collaboratively to not only implement smokefree policies and help staff and patients and their families to quit smoking in their own health-care facilities but to also advocate for this to be a national requirement.

Tobacco free health care policy: a case study from Indonesia

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Introduction: Smoking kills 200 000 annually and more than 97 million Indonesian non-smokers are regularly exposed to secondhand smoke (SHS). Indonesia has a national ban on smoking in healthcare facilities and educational facilities and on public transportation, however, enforcement is weak.

Objective: Explore integration of tobacco free healthcare into comprehensive smoke-free policy of Bogor city.

Approaches:
  i) National: a) Included smoke-free and warn about dangers of tobacco into Health Law

2009. The law yet to be enforced. b) Ministry of Health (MOH) initiated integration of tobacco control into the health system and sensitizing policy makers on ways to improve lung health
  ii) Sub-national: Initiated smoke-free. Bogor city is the first demonstration site of the comprehensive smoke free policy

Results: MOH issued a ministerial decree to strictly enforced smoke-free health care and developed a national smoke-free guideline. Bogor city government adopted 100% smoke-free local law. The law bans smoking in all public places, work places and public transports. The law also bans tobacco advertisement, promotion, sponsorship and selling in health care premises. The city health department initiated warns visitors about dangers of tobacco use, exposure to SHS and provides brief advice to quit smoking through primary health care. Observed encouraging enforcement with more than 90% compliance to the law in health care facility.

Conclusion: Bogor city has demonstrated a model of comprehensive tobacco free health care. The model can be expanded in other settings.

Smokefree healthcare in Russia: mission impossible?

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In Russia, smoking causes about a half of a million deaths each year. According to the WHO, 60% of Russian men smoke, and the number of female smokers has been increasing steadily since 1991. The rate of smoking amongst health care professionals exeeds 20%. Smoke-free health facilities in Russia are scarce. Despite existent legislation that forbids smoking in all health institutions, smoking is still evident. In March 2010 the first Smoke-Free Health Care project was initiated in Krasnoyarsk, Siberia under the Union grant. The project goal is to totally ban smoking in all regional medical facilities by implementing the Decree of the Regional Health Ministry. The baseline survey conducted smoking prevalence amongst medical personnel is higher than the national level, 40, 1% (63.3% for men and 17.0 % for women). In April 2010 the project staff conducted a baseline survey amongst the head doctors of the regional health facilities to evaluate their attitudes towards the smoking ban and to estimate the compliance with the current smoking regulations. The study showed that the majority of medical professionals (65.6%) approved complete smoking ban, and only 15% thought that smoking could be allowed indoors. Just 24% of facilities had clearly marked places for smoking.

Formally 77.4% of facilities surveyed had signage forbidding indoor smoking, but in more than half of cases (55.9%) there were evidence of hidden smoking places. The coverage of different prevention methods (counseling, support and treatment) varied from 25.5% to 43%. Despite high smoking prevalence among medical professionals, there is a strong support for 100% smoke-free medical facilities implementation among them. 'Siberian variant' represents the first regional project in Russia. Based on this pilot project the guidelines for smoke-free hospitals implementation will be developed for SF HC replication on regional and national level.

Smokefree healthcare policies in the Middle East: between potential success and predictable conflicts

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Health care facilities are one of the most influential settings for modeling abstinence from smoking and promoting smoke-free environments (SF). Health professionals have a prominent role to play in tobacco control and to support countries to fully implement the FCTC. In many countries of the Middle East, the enforcement of SF policies in health care settings remains an unresolved challenge. The recent statistics in GATs 2010 reflects the current situation where almost half of the visitors of health care facilities are exposed to the deadly second hand smoke. Egypt and Pakistan are among the countries that have the highest tobacco prevalence. In both countries laws on SF policies are enacted yet they have not been enforced across the society. Poor enforcement has been attributed to lack of awareness about the existing laws amongst the public including health professionals, as well the enforcers. In addition there is, limited knowledge of enforcers on the effective enforcement mechanisms and protocols and lack of human and financial resources. Despite the aforementioned challenges, in Egypt there is a current momentum to effectively enforce SF policies under the smoke-free cities initiatives lead by the MOH. In Pakistan too, the MOH has undertaken an initiative to enforce the SF law in letter and spirit and health care facilities are amongst the top priority. IEC material has been developed under the BI grant and orientation sessions organized for hospital administration to create awareness leading to effective enforcement of the law. In both Egypt and Pakistan, the MOH in collaboration with The Union is undertaking active steps to build national capacity required to carry on this initiative with a primary focus on health care setting. This includes provision of technical assistance, training of officials and enforcers and sharing and dissemination of information on best practices worldwide.

NAP AND NTP: ESTABLISHING PARTNERSHIPS TO ACCELERATE INNOVATION FOR TB-HIV COLLABORATIVE ACTIVITIES

Research to reduce the burden of TB by providing IPT to PLWH

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Since 1998, WHO and UNAIDS issued the policy statement on IPT for PLHIV. Yet, there was no progress to implement IPT during the last decade. In 2008, WHO recommended to scale up the 3 Is for PLHIV, including IPT. Globally, providing IPT within the countries' program conditions is not common. In this symposium, we present the process and outcome of research on IPT for PLHIV in Chiang Rai, the northernmost province with high HIV and TB prevalence of Thailand. Since the epidemic of HIV in Chiang Rai in 1993, the Research Institute of Tuberculosis, Japan Anti-tuberculosis Association (RIT-JATA) in collaboration with the community hospitals, the provincial hospital in Chiang Rai and the Ministry of Public Health have implemented the research on IPT. We summarize the outcome in the Table. The knowledge and experiences gained from the research have been transferred to other hospitals in Chiang Rai and other provinces in the Northern region. Moreover the IPT research has contributed to the formulation of Thailand's guideline on IPT.

Year of research implementation/ year of publication	Area of research on IPT and study population	Results	Implication for policy and or practice
November 1993– August 1994 (AIDS 1997; 11: 107–112)	Adherence to 9-month IPT among 463 PLHIV in a provincial hospital	Adherence rate = 67.5%. Reasons of non-adherence were identified	Recommendations for improving adherence to IPT
1995–1999 (AIDS. 2001 Sep 7; 15(13): 1739–41)	Risk of default to IPT among 412 PLHIV in a community hospital	Default rates decreased from 57% in 1995 to 17% in 1999 due to the contribution of PLHIV-volunteers	PLHIV volunteers can contribute to ensuring adherence to IPT
2004–2009	Impact of IPT, ART and IPT plus ART on TB incidence	The preliminary analysis will be presented in the symposium	IPT reduce risk of TB among PLHIV

INNOVATIONS IN RESEARCH: DIAGNOSIS, TREATMENT AND INFECTION CONTROL FOR MDR-TB

Operational research in infection control for ambulatory treatment of MDR-TB

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The emergence of drug resistant TB (MDR and XDR-TB) have prompted new interest in TB infection control globally. However, interventions to reduce the risk of TB transmission are needed in high TB burden settings regardless of the prevalence of drug resistant TB, particularly in high HIV settings. Community based treatment of drug resistant TB is essential if we are to scale up treatment globally and impact on this emerging epidemic. Strategies to reduce the risk of TB transmission prior to diagnosis and during treatment are needed to complement community-based treatment. There is, however, a lack of evidence-based interventions for TB infection control, particularly in resource-limited settings. This presentation aims to describe current operational research in TB infection control and what is needed to support scale up of drug resistant TB treatment in high burden settings.

Efficacy of second-line anti-tuberculosis drugs: comprehensive review of in vitro, animal and clinical evidence

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Drug-resistant tuberculosis (DR-TB) is a global health threat, with an estimated 440 000 new cases of MDR-TB and 25 000 cases of XDR-TB emerging per year. Treatment of DR-TB is hindered by the high toxicity and poor efficacy of second-line TB drugs, as well as the lengthy treatment duration needed for sustained cure. Clinical trials to determine the most efficacious combination of new or existing TB drugs are sorely needed but are lacking. To determine the best way to use new drugs in the pipeline for the treatment of DR-TB, it will first be necessary to optimize regimens of available second-line agents. This presentation will summarize past and present in vitro, animal, and clinical data regarding currently-available agents that may have activity against MDR- or XDR-TB, focusing on the contributions of individual agents to multi-drug TB therapy and current and future research priorities. Drugs or drug classes that will be reviewed include aminoglycosides, capreomycin, fluoroquinolones, ethambutol, pyrazinamide, ethionamide, para-amino salicylic acid (PAS), cycloserine, terizadone, beta-lactams, macrolides, clofazamine, and oxazolidinones.

GLOBAL LABORATORY INITIATIVE

Strengthening the SRL network

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The TB Supranational Reference Laboratory Network (SRLN) was created in 1994 in order to support the WHO-IUATLD Global Project on TB drug resistance surveillance. The original terms of reference required that each of the SRLs had a permanent functional TB laboratory providing quality culture and drug susceptibility testing (DST), with a commitment to support at least two countries with DST proficiency testing (PT), to provide external quality assurance during drug resistance surveys, and to provide training on culture and DST in relevant countries as needed. Between 1994 and 2009, the SRLN was expanded to 29 laboratories, largely driven by regional initiatives and institutional interest in joining the network. The SRLN continues to be the backbone of the Global Drug Resistance Surveillance Project; however, given the pressing need for scaling up laboratory services an expanded focus for SRL activities is urgently needed. Despite being a great technical resource for laboratory scale-up and capacity development, the SRLN is generally under-utilised, largely due to a crucial lack of funding and human resource capacity. While there is a skewed concentration of SRLs in Europe there are only three SRLs in Africa, where the need for laboratory strengthening is most pressing. In addition, very few SRLs are linked to francophone and lusophone-countries. In April 2010, a Global Consultation of the SRL Network was convened at WHO in Geneva, Switzerland where revised TORs and eligibility and inclusion criteria were developed and endorsed by the entire network. In addition, a process was developed for new candidate SRL to establish formal links with exisiting SRLs as an essential step towards their eventual designation as an SRL. The final versions of these documents can be accessed via the GLI website http://www.stoptb.org/wg/gli/. Recognizing the importance of the SRLN in global laboratory strengthening efforts it has been designated as a sub-group of the GLI

TB biosafety guidance

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Infections with *Mycobacterium tuberculosis* are a proven hazard to laboratory personnel as well as others who may be exposed to infectious aerosols in the laboratory. The risk of infection can be minimized through the application of the appropriate biosafety and containment principles and practices. Determining the appropriate biosafety level is based on a risk

assessment which takes into consideration the pathogen, mode of transmission, the nature of the materials being manipulated, and the experimental manipulations. *Mycobacterium tuberculosis* is a Risk Group 3 pathogen transmitted by the air-borne route. Exposure to laboratory-generated aerosols is the most important hazard encountered. Based on the outcomes of two Expert Group meetings on TB laboratory biosafety requirements sponsored by WHO, GLI, and CDC, consensus interim recommendations have been made for minimum biosafety requirements for TB testing including 1) direct AFB-smear microscopy; 2) processing specimens to concentrate bacilli for smear, culture, drug susceptibility tests, and molecular tests; and 3) manipulating cultures for smear, subculture, identification, drug susceptibility tests, and molecular tests. The recommendations will be incorporated into a revision of the WHO TB Biosafety manual.

Progress with implementation of new tools

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During the last few years, there has been remarkable progress in the implementation of new TB diagnostic tests in high-TB burden countries. Driven by the need for improved diagnostics to address M/XDR-TB and TB-HIV, the Stop TB Department at WHO has implemented a process for issuing guidelines on new TB tools. This process begins with the identification of a need for policy change, reviewing published and unpublished data, convening an expert panel to review the evidence and draft a policy recommendation, approval of the policy guidance by STAG-TB, and formulating and disseminating the new policy. Since 2007, WHO has issued recommendation on the use of TB liquid culture and DST, rapid TB species identification, molecular line-probe assays for rapid screening for MDR TB, non-commercial culture and DST systems, LED fluorescence microscopy, and same-day microscopy for TB diagnosis. In 2010, WHO will also convene expert panels to consider guidance on automated molecular testing for TB and rifampin-resistance, a line-probe assay for XDR TB, interferon-gamma release assays, and commercial serologic tests for TB. At the same time, significant financial resources are now available for TB laboratory strengthening and scale-up of WHO-recommended diagnostic technologies. Implementation of these new tools is being facilitated by several initiatives, including EXPANDx TB (a collaborative effort of GLI, FIND and WHO/GDF funded by UNITAID), TREAT TB (a Union initiative funded by USAID), and the Implementing New Approaches and Tools (INAT) Sub-Working Group of the Stop TB Partnership. This presentation will include an overview of these new diagnostic technologies and an update on implementation efforts.

ADDRESSING HUMAN CAPACITY DEVELOPMENT REQUIREMENTS FOR SUSTAINABLE IMPROVEMENTS IN CONTROL AND TREATMENT OF TB

Training of microscopists to address increased laboratory needs in Zambia

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Introduction: Task shifting has been acknowledged as an important approach the chronic shortage of skilled health staff. It involves shifting of specific tasks from appropriately qualified staff to health workers with lower qualifications. The shortage of skilled workers is particularly more serious in developing countries with a high TB and HIV burden such as Zambia. The burden of TB can be reduced by reducing transmission through improved detection and treatment of infectious cases. This can be achieved with increased access to TB screening and sputum microscopy. However, access is affected by shortage of laboratories and personnel.
Methods and results: ZAMBART project and Zambian MoH piloted two interventions to address shortage of health workers at busy TB diagnostic health facilities. The first involved providing access to screening services involving lay community members and the second involved training school leavers as TB microscopists to conduct TB smear microscopy. TB screening services improved with over 50% of suspects submitting sputum samples via the first intervention. During an evaluation of the second intervention, 13 out of 14 microscopists attained a score of more than 80%. Microscopists employed correct smearing and staining procedures and read the smears correctly.

WHO Collaborative Network on Pre-service Education Content: a public health approach

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To address the human resource needs to support rapid expansion of TB-HIV services within primary health care, there is an urgent need to improve pre-service preparation of medical doctors, clinical officers, and nurses in limited-resource countries. A collaborative network has been established to develop, update and share pre-service education content compatible with WHO guidelines and public health approach for TB, HIV, malaria, maternal and child health, and sexual and reproductive health. The goal

is to support faculty access to competency-based learning materials with appropriate content and methods so that health care workers are able to provide quality patient care compatible with a public health approach upon graduation, joining clinical teams at health centres and district hospitals, without further in-service training. The collaboration is based on the WHO Integrated Management approaches for Childhood Illness (IMCI), Adolescent and Adult Illness (IMAI) and Pregnancy and Childbirth (IMPAC) and supports the Stop TB Strategy. The network builds on the extensive experience integrating IMCI into pre-service education and the work of collaborating network partners in improving preservice curricula.

The network affinity groups address both core competencies as well as methods to most efficiently and effectively transmit these to students—case-based learning; student assessment tools; computer-based learning; clinical practice; expert patient trainers (exploring potential transformative effects on education of their inclusion on faculties), skill stations/simulations, audiovisual materials, job aids, textbook chapters—as well as faculty development. Emphasis is placed on how pre-service education can support the priorities, standards, tools and approaches of the national Ministry of Health for decentralized delivery of services at district level. Materials are shared at http://my.ibpinitiative.org/preserviceducation (request access imaimail@who.int).

Integrating tuberculosis into schools of public health core curricula

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Objectives: It is essential to sustain a public health workforce able to implement and advance strategies in order to treat, control, and ultimately eliminate tuberculosis (TB). However, TB is not consistently addressed in the curricula of most U.S. public health programs. This project is sponsored by the Global Tuberculosis Institute (GTBI) one of 4 CDC-funded Regional Training and Medical Consultation Centers in the U.S. TB control staff and other experts worked with faculty from schools of public health to develop educational materials that directly address established public health core competencies.
Methods: The TB Curriculum Development Group created teaching materials using a systematic process:

needs assessment; materials development; field-testing; implementation; and evaluation. An online evaluation instrument is available to elicit continuous feedback to revise and update materials. Student and Instructor versions are available on the GTBI website at http://www.umdnj.edu/globaltb/products/incorporating.html. A form to request Instructors' versions of materials was developed to track use of materials. Announcements describing the curriculum materials were sent to all accredited US public health schools, programs and TB Control Programs.
Results: Curriculum materials were posted on the GTBI website in December 2009. Between December 2009 and early July 2010, the website page was visited 1617 times. Twenty-two requests for Instructors' versions were made; 12 came from academic settings and 10 from public health organizations. Seventeen were for public health education and training and 5 for clinical training. Sixteen were for use in the U.S. and 6 in international settings.
Conclusions: Materials developed through this project can add important and often neglected content on TB to public health core curricula and can help to build capacity for public health professionals working in TB control.

Development and implementation of the TB curriculum coordinating centre

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Setting: The National Tuberculosis Curriculum Consortium (NTCC) was established by NIH/NHLBI in late 2003 to improve teaching of tuberculosis to students of medicine, nursing and allied health fields. Funding for the project was provided through April 2010.
Background: Over 50 professors were recruited for their expertise in tuberculosis, education, and/or academic administration. Each represented one or more of eight disciplines: Medicine, Baccalaureate or Advanced Practice Nursing, Pharmacy, Respiratory Therapy, Physician Assisting, Clinical Laboratory Sciences, and Public Health. Core Competencies were developed and published. A 2005 Needs Assessment was performed. It included 1480 students in 20 NTCC schools. Knowledge, skills, and attitudes about tuberculosis were assessed in order to direct the NTCC's educational content.
Website: The primary work of the NTCC was to develop educational materials and present them to the community of teachers through a website which evolved to the Educational Product Center (EPC) and is a repository for on line case based educational resources about tuberculosis that could be accessed by faculty, students, and the public free of charge. Principles of active learning and associated methodologies were used throughout the tenure of the project. The website is now the NTCC EPC with Online Learn-

ing Modules of Computerized Cases, a Multimedia Resource Bank, a Question and Answer Bank, and a Clinical Case Description Bank. By April 2010, there were about 3000 registered users representing 73 countries and utilization exceeded 25 000 downloads/executions of materials. The website will continue for at least one year under the auspices of the UCSD Office of Educational Computing.

Summary: We believe the NTCC carried out the mission of the NIH/NHLBI in the development and implementation of the National Tuberculosis Curriculum Consortium and urge that you visit the website (http://ntcc.ucsd.edu).

RESEARCH CHALLENGES TO IMPROVE CASE MANAGEMENT AND REDUCE MORTALITY IN CHILD PNEUMONIA

Causes of child pneumonia and challenges for aetiology research

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Accurate data on childhood pneumonia aetiology is essential especially from regions where mortality is high, in order to inform case-management guidelines and the potential of prevention strategies such as bacterial conjugate vaccines. However, this information is scanty because the yield from blood culture is low. Lung aspirate culture provides a higher diagnostic yield. We aimed to determine if diagnostic yield could be increased further by polymerase chain reaction (PCR) detection of bacteria and viruses in lung aspirate fluid. This improved diagnostic yield significantly and confirmed *Streptococcus pneumoniae* as the commonest bacterial organism causing radiological pneumonia. Procalcitonin reliably differentiates viral from bacterial pneumonia.

Research in high mortality setting and impact of HIV

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Pneumonia is the major cause of death in children worldwide, including in HIV endemic communities. A recent meta-analysis found that HIV infection was associated with a six-fold increased risk of death in African children with severe pneumonia managed according to recommended case-management strategies. The increased risk of death is particularly in HIV-infected infants (already a high-risk group for pneumonia incidence and mortality). Pneumocystis pneumonia is a major cause of death in HIV-infected infants not receiving cotrimoxazole preventive therapy. The incidence of bacterial pneumonia is much higher in HIV-infected infants and children. Other likely important pathogens identified by clinical and autopsy studies include tuberculosis and cytomegalovirus. Barriers to establishing aetiology of child pneumonia remain especially in resource-limited setting where the majority of cases occur. Case-management guidelines are being formulated without a strong evidence base. Available preventive and treatment strategies have huge potential to reduce the burden and deaths due to HIV-related child pneumonia but implementation is a challenge. The role of past and future research to improve management of child pneumonia in HIV-endemic setting will be the focus of this presentation.

ZOONOTIC TB: PUBLIC HEALTH AND SOCIO-ECONOMIC CHALLENGES: PART 2

The importance of extra-pulmonary tuberculosis caused by *Mycobacterium bovis*: developing a guinea pig model using the oral route of infection

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Background: With *Mycobacterium bovis* (*M. bovis*) 're-emerging' as a cause of human tuberculosis (TB) in some areas of the world, and the growing scientific evidence indicating that the true incidence of human TB caused by *M. bovis* is underreported, there is a need to develop appropriate animal models to investigate the unique extra-pulmonary lesions associated with *M. bovis* infection in humans. Based on our experience with the low dose aerosol infection of guinea pigs with *Mycobacterium tuberculosis*, we propose to characterize the guinea pig model oral *M. bovis* infection to screen antimicrobial drugs intended for use in humans.

Objectives: 1) To develop a reproducible oral infection model of guinea pigs with the Ravenel strain of *M. bovis* using milk as a carrier. 2) To evaluate the pathogenesis generated after orally challenging guinea pigs with infective doses of *M. bovis*.

Approach/methods: Experimental infection of immunologically naïve guinea pigs with 2 doses of virulent strain of *M. bovis* by the oral route to mimic natural infection.

Expected outcomes: As seen in extra-pulmonary TB caused by *M. tuberculosis*, we anticipate that similar lesions in guinea pigs infected via the oral route will be refractory to combination antimicrobial therapy.

Relevance: These data will provide a new under-

standing of the pathogenesis of *M. bovis* extra-pulmonary infections and the importance of this specific lesion type in treatment failure in humans.

Long term goals: To use this model to evaluate different antimicrobial drugs used for the treatment of TB in humans, and the efficacy of these drugs for the treatment of TB caused by *M. bovis*.

The science and the politics of bovine TB in the United Kindgom

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Bovine tuberculosis has been eradicated in many countries around the world, notable exceptions being the UK, Ireland, New Zealand and the USA. These countries all have the presence of a wildlife reservoir of *Mycobacterium bovis* infection in common. The UK has had to invest large sums into research attempting to come up with solutions to the disease problem. A key question remains whether wild badger populations need to be reduced in density in order to make significant progress towards eradication of the disease. There is strong disagreement between different stakeholder groups in this respect, which could not even be resolved by a large randomised controlled field trial that cost over £40Mill and was conducted between 1998 and 2007. The scientific evidence generated by this study did not allow government policy makers to make a clear decision. It was therefore decided by the previous Labour government to invest in badger vaccine development, rather than to permit population reduction of wild badger populations. At the same time the Welsh Assembly government decided to employ such population reduction methods, but has so far been prevented to do so as a result of legal challenges. In the meantime cattle tuberculosis reactor rates have increased in England at a slow but steady rate. The current UK government is now reviewing the policy.

Prevalence of bovine tuberculosis and molecular characterisation of isolates from cattle of a dairy farm in Bangladesh

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Background: Like other animals, bovine TB has not been properly reported in many developing countries including Bangladesh. Previous studies based on tuberculin skin test indicates that bovine tuberculosis exists in Bangladesh. However, there is a paucity of recent information about bovine TB and its causative agents in Bangladesh.

Objectives: a) Tuberculin skin test of cattle; b) isolate causative organism from TB suspected cattle; c) conventional and molecular characterization of the isolates; d) anti-TB drug susceptibility testing, and e) genotyping.

Methods: Prevalence of bovine TB was surveyed using tuberculin skin test (TST). Suspected cattle were sacrificed and vital organs were physically examined and processed following standard bacteriological technique to isolate mycobacteria on Löwenstein-Jensen (L-J) slants. Mycobacterium-suspected strains were screened for acid fast staining (AFB), sensitivity to P-nitro benzoic (PNB) acid, TCH, streptomycin, isoniazid, rifampicin and isoniazid. For molecular characterization, RD analysis was performed for cfp32, RD1, RD4, RD9, and RD12; single nucleotide polymorphism for the gyrB, mmlp6, TbD1and PPE55 genes. Genotyping was performed by standard spoligo- and VNTR MIRU typing.

Results: Out of 187 cattle, 17 reacted with TST. Twenty-one TB suspected cattle were sacrificed. Physical examination revealed prominent nodulation mostly on the lung and liver. Histopathology of the nodulated tissue revealed TB of cattle. Strains were sensitive to all first line anti-TB drugs. Prominent AFB staining, sensitivity to PNB indicated that the strains were members of *M. tuberculosis* complex. Molecular characterization and genotyping indicates that the stains are similar to *M. africanum* similar to Oryx bacilli.

Conclusion: Cattle infection with *M. africanum* Oryx bacilli is surprising and possible origin is unknown. Further study is needed to find out the probable source of infection.

Mycobacterium bovis in human cases of tuberculosis: a review

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Transmission of tuberculosis from cattle to humans has been known to occur for a long time; however, after implementing pasteurization of milk, the epidemiological role of *M. bovis* in human cases declined. Nevertheless, reports from the past few years indicate that the problem has re-emerged, especially in high risk populations: people with the HIV virus or diabetes and people from developing countries where TB in cattle is common. Milk and fresh cheese have been frequently associated to infections, especially fresh cheese from which *M. bovis* has already been isolated. In San Diego, 129 TB-isolations, out of 1931, were *M. bovis*; the main site was extra-pulmonary. Fresh cheese was also suggested as the main source of infection where *M. bovis* accounted for 45% (62/138) of all culture-positive cases in children under 15 and 6%

(203/3153) of adult cases, and reported as the most probable source of infection in an outbreak in children in New York City. In France, the incidence of cases by was related to occupational exposure and ingestion of unpasteurized milk. The arrival of molecular techniques has enormously facilitated the task of relating cases of TB to *M. bovis*. The role of *M. bovis* as cause of TB is underestimated because the disease caused by *M. bovis* is clinically indistinguishable from that caused by *M. tuberculosis*, the diagnosis requires isolation facilities and specific identification of the bacteria, there is no interest in typing isolates and there is no accurate *M. tuberculosis* complex speciation. There is a general belief that the source of infection is related to the type of TB: *M. tuberculosis*, usually inhaled, leads to primary pulmonary lesions while *M. bovis*, usually acquired by consumption of contaminated milk, is more likely to cause non-pulmonary lesions. Therefore, *M. bovis* is rarely searched in pulmonary TB. However, it seems that *M. bovis* is more frequent in human TB than usually believed.

Mycobacterium bovis in Tunisia: location and resistance profile to antibiotics

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Bovine tuberculosis, caused by *Mycobacterium bovis* is a zoonotic infection that also affects humans. The consumption of unpasteurized milk or dairy products as well as close contact with the infected animals plays a major role in the spread of the disease. In this study, we report 22 cases of human tuberculosis where *M. bovis* was isolated. Most of the clinical samples were obtained from lymph nodes ($n = 18$). Other samples were 2 sputa, one mammary tumefaction and one cutaneous suppuration. The age of the patients varies from 5 to 47 years. Acid-fast bacilli identification was negative at the majority of cases. The culture on Löwenstein Jensen medium allowed isolating *M. bovis* within 42 to 60 days. The biochemical identification was confirmed by a molecular method (Genotype MTBC, Hain LifeScience). 20 strains were susceptible to antituberculous drugs. Two strains isolated from chronic lymphadenopathy were resistant, one was monoresistant to rifampicine and another was multidrug resistant (SHRE). The incidence of bovine tuberculosis is not well evaluated in Tunisia. Epidemiological and public health aspects should be analyzed to control the disease in humans and animals.

SYMPOSIA: SUNDAY 14 NOVEMBER 2010

FIXED-DOSE COMBINATIONS: PAST INTRODUCTION AND FUTURE INNOVATION

Pathway to adoption of FDCs in China's national TB control programme

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TB FDCs have been available in China since the 1990s. Chinese researchers have evaluated the safety, effectiveness, and acceptability of using FDCs. Recently, the Chinese Ministry of Health (MOH) developed a plan to adopt and expand the use of TB FDC's in the NTP. Although the pathway to adoption of TB FDCs starts with a commitment by the MOH to use FDCs in the NTP, the pathway also involves working with drug manufacturers, SFDA, the Ministry of Finance (MOF), and the CDC system. At present, 17 TB drug manufacturers are producing 4 types of FDCs (HRZE, HR, HRZ, HRE) using 7 different dosage formulations. According to the current market price for TB FDCs in China, if the use of FDCs is extended to the entire NTP, an additional 140 million RMB will be needed every year. At the same time, as more drug manufacturers produce TB FDCs and the drug volume increases, we expect price of FDCs to decrease. The SFDA is working to improve the quality-standard of TB FDCs. The pharmacopeial monographs for TB FDCs are being revised, SFDA is strengthening the GMP inspection of manufacturers producing TB FDCs, and a system for monitoring the post-production quality of FDCs is being developed. WHO is working with interested drug manufacturers to improve manufacturing practices for TB FDCs and to prepare dossiers for WHO prequalification. The MOH plans to expand the use of TB FDCs to more than 90% of the country in 3–5 years. To achieve this target, several challenges confronting the adoption of TB FDCs in China have to be simultaneously addressed. The pathway that has been developed seeks to address these challenges.

Assuring quality of FDCs: challenges and solutions

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Global initiatives such as the WHO Prequalification of Medicines Programme contribute to assure the quality of anti-tuberculosis fixed dose combination

medicines (FDCs), particularly in support of public programs. In many countries, prequalification of suppliers and products contributes to ensure that procured FDCs reaching patients are safe, effective and of appropriate quality. This may often screen out unreliable manufacturers and suppliers, but some prequalified products may still fail to comply with specifications (packaging, labeling, and specified pharmacopoeial standards) and performance (reduced bioavailability and instability of FDC formulations). At country level there is need to implement effective programs that combine rigorous evaluation of manufacturer/ supplier and product documentation; inspection of relevant facilities for Good Manufacturing Practices, Good Warehouse and Distribution Practices, appropriate retail and dispensing; risk-based sampling and testing to verify compliance with standards; and health care provider and consumer reporting of product problems. Moreover, a country's quality assurance system is only as effective as its ability to take action and enforce quality standards. Many countries often lack the necessary resources to implement effective and sustained programs based on complex and expensive technologies. A three tier testing strategy is recommended for building and optimizing product quality testing capacity and efficiency. Quality assurance is a shared responsibility and the roles of the various stakeholders need to be clearly established. Above all, it takes strong political will to mobilize adequate and sustainable financial resources and to enforce quality standards that serve the public health.

FDCs in the public sector: adoption and quality

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The Clinton Health Access Initiative (CHAI) examined a ten-country sample of public TB programs (China, Ethiopia, India, Indonesia, Kenya, Nigeria, Rwanda, South Africa, Uganda, and Vietnam) to determine whether fixed-dose combinations (FDCs) were the predominant form of treatment in these programs, and the quality standards under which TB medicines were procured. This examination was conducted through phone and in-person interviews with national tuberculosis program (NTP) managers, other NTP personnel, and outside experts, and analysis of 2009 data on drug value provided by NTPs and others. In every country examined except India (which prefers co-blistered single-drug pills) and China (which is now migrating to FDCs), the public TB treatment program was indeed structured around FDCs. Over 70% of the total value of medicine in the countries examined, however, was procured through tenders that specify quality-assurance levels that are less stringent than those required by the Global Drug Facility (GDF). CHAI's examination found that a country's decision on whether to enforce stringent

(i.e., GDF-equivalent) quality standards in TB medicine procurement was closely correlated to the source of funds for that procurement, as well as whether
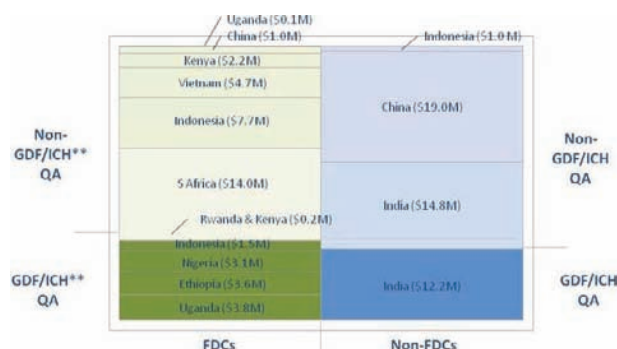
GDF was involved. When Global Fund financed medicine procurement, and/or when GDF was involved in that procurement, stringent quality standards were required for all procured medicines. When countries procured medicines with their own funds or with funding from sources other than the Global Fund or GDF, meanwhile, required quality standards tended to be less stringent than those specified by GDF. This tendency may be driven, in part, by national preferences for sourcing medicines from local manufacturers who may not be able to achieve the highest levels of quality stringency.

FDCs in the private sector and incorporation into new regimens

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The size and characteristics of the private TB drug market remain largely unknown. We used IMS Health data to analyze private TB drug consumption for the 10 high burden countries where IMS has data and in which a significant private TB drug market is thought to exist. The overlap between the private market (defined for this study as any market not supervised by the national TB program) and IMS data was first determined. Private markets in India, Indonesia, the Philippines and Pakistan were found to supply enough first line TB drugs to make up standard 6–8 month regimens for 65–115% of the respective countries' incident cases. First line TB drug volumes in the private sector were largely stable over the past 5 years. Consumers in five of the countries (India, Pakistan, Philippines, Bangladesh and South Africa) used predominantly fixed dose combinations (FDCs) in the private market; those in the other five countries (China, Indonesia, Russia, Thailand and Viet Nam) used predominantly loose drugs. Prices for FDC-based and

loose-drug-based regimens were more similar to each other in the FDC-predominant countries. Diversity of drug strengths was high for both loose drugs (7–26 distinct dosage strengths per country) and FDCs (2–57 dosage strengths per country), with many forms diverging from WHO and NTP recommendations and diversity being highest in India. The number of manufacturers with >3% market share ranged from 2–11 per country, and manufacturing was concentrated amongst fewer companies for FDCs than for loose drugs. These FDC manufacturers represent potential producers for new FDCs, in which new drugs could be incorporated as they are approved for use against TB, although the possible need to combine weight-banded and non-weight-banded drugs will constitute a challenge for such development.

TUBERCULOSIS INFECTION CONTROL

TB infection control and operational research in China

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In China, tuberculosis (TB) ranks as the leading cause of death from infectious disease, with over 1.3 million people developing active TB each year. TB infection control, however, is still at an early stage in China. More than 90% of the world's TB cases are found in healthcare facilities in developing countries and China is no exception. Many of the facilities in China lack the policies and resources for implementing effective TB infection control programs. One study has found that healthcare workers (HCW) in China have a significantly higher rate of TB infection than the general population. To address this challenge, the China National Center for TB Control and Prevention in collaboration with the US CDC and WHO have developed the 'China Tuberculosis Infection Control Manual'. This manual contains detailed instructions on TB infection control practices in the different pertinent settings. Although HCW have been widely considered as a high risk group for contracting TB, very little research has explicitly focused on TB infection and disease rates among HCW in China. The China CDC in partnership with U.S. CDC has begun an operational research project to evaluate the acceptance, comprehension and feasibility of the TB infection control manual. This study also aims to determine the prevalence of TB infection and disease among HCW in China as well as understand the current general situation of infection control in China.

The results of this study are expected to enhance the usability of the manual, and minimize the risk of TB transmission in health care settings in China.

Community perspective: involving the community in implementing TB IC policy

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Khayelitsha is a large urban township in Cape Town with an estimated population of half a million people. Khayelitsha has an extremely high burden of HIV infection, tuberculosis and additionally drug resistant TB (DR-TB). A pilot programme to decentralise the care and treatment of DR-TB was implemented from 2007. TB infection control is a central part of this programme. TB infection control activities are needed for health care facilities, in the homes of patients with DR-TB and in community congregate settings. Different strategies are employed in each of these settings, but with the overall aims of increasing knowledge and understanding of TB transmission and reducing transmission risk. Reducing stigma associated with MDR and XDR-TB is also key to infection control activities. To achieve these aims, community based organisations have been trained and involved in TB infection control. Producing lasting behavioural change is necessary to reduce the risk of TB transmission —involving community organisations is central to achieving this. Preliminary experience and ongoing plans will be presented.

National perspective: rolling out a national TB IC policy in the context of ART scale-up

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Rationale: In Tanzania the co-epidemics of TB and HIV have overwhelmed the health care system, with a significant deleterious impact on TB infection control. **Methods:** ICAP Columbia University has supported MOH to develop and roll out a nationwide TB Infection Control policy and evaluation process. In 2008, a TB IC monitoring form was field tested; on 2009, district/HF managers, HIV-TB coordinators, HIV-TB focal persons from 120 HFs in 3 regions were trained. The TB IC monitoring tool was used to assess the implementation of TB IC policies in 10 sites at baseline and at two subsequent visits in the following 2 quarters. **Results:** During the assessment the TB IC written plan was found to be available at 90% of sites. The proportion of sites that had a triage policy at HIV clinics was initially low (40%), increasing to 100%

at follow up, as well as the implementation of cough hygiene policy at HIV clinics' waiting areas. The proportion of sites having nurse referring coughers at HIV clinics to Lab, before entering the examination room, increased (20% vs 100%). Proportion of sites having TB IC posters displayed and conducting TB IC education went from 14% at baseline to 70% at follow up. Proportion of sites collecting sputum samples in open air at wards, where 50% of the in-patients are HIV positive in Tanzania, increased from 27% to 50%. Proportion of sites separating PTB patients from other in-patients in the ward went from 0% to 40% at follow up.

Conclusions: An improvement on implementing TB IC measures was demonstrated, especially at HIV clinics. TB screening and PTB separation in the wards were found still low at follow up assessment. The same monitoring over time will be extended to additional high volume sites and the 3I's training including TB IC will be rolled out country wide.

The importance of administrative and managerial support in implementing TB IC

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Aim: To demonstrate the importance of administrative and managerial support in implementing effective TB infection control measures in a rural and resource-limited hospital.

Setting: The Church of Scotland Hospital is a 347 bed rural district hospital in Tugela Ferry, KwaZulu-Natal, South Africa. It experienced a drastic rise in the incidence of XDR- and MDR-TB which has been associated with nosocomial infection.

Domains of infection control: Administrative, environmental and personal protection.

Results: Infection control interventions were informed by international guidelines and local research. Various interventions were initiated by management, including new policies, mechanical ventilation, improved patient care and education. These interventions further resulted in improved health promotion, staff training and addressing high risk areas. These steps helped to decrease the nosocomial TB transmission risk.

Conclusions: The involvement, support and buy-in of the executive management resulted in an improved TB infection control program with a significant reduction in nosocomial TB transmission risk.

Tuberculosis infection control: from global policy to country implementation

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Background: Global awareness of preventing tuberculosis (TB) transmission in health-care facilities and communities increased steadily recently, following X/MDR-TB outbreaks and discussions in international forum. However, scaling-up TB Infection Control (IC) measures at country level remains a challenge.

Objective: To analyse major components of the Global Policy on TB-IC, and to describe strategies for scaling-up TB-IC measures at country level.

Results: TB-IC measures are essential to reduce transmission and protect health care workers. Early diagnostic and prompt treatment of TB drug-sensitive or X/MDR-TB patient is essential to interrupt TB transmission, but it is not always possible. Simultaneous implementation of simple IC measures, as described in the recent WHO guidelines (2009), is necessary. TB hospital wards and congregate settings need to implement IC measures (administrative, personal protection, environmental). However, an emphasis and a prioritization should be done on implementing first simple and economical administrative measures, e.g. identifying potentially infectious cases (triage), separating them, enhancing the use of mask, minimizing the time spent in health care settings and assuring HCW protection. These procedures have to be context-sensitive and prevent stigma. In addition, TB-IC should not be viewed as a 'stand-alone' action. Embedding TB-IC within the broader contexts of the Stop TB Strategy, overall IC and health system strengthening, should allow its integration into broader national plans. Preliminary data on country implementation, existing bottle-necks and opportunities for countries eligible to apply to Global Funds and other donors will be presented.

Conclusions: Using first simple and economical TB-IC measures, together with embedding TB-IC within broader plans, should contribute to their step-wise implementation. This should also ultimately impact positively the country TB burden.

MICROBIAL, ENVIRONMENTAL AND HOST FACTORS IN THE PROPAGATION OF DRUG-RESISTANT TUBERCULOSIS

Population genomics, fitness and the microevolution of drug resistance

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Antibiotics exert a massive selective pressure on the evolution of *M. tuberculosis*. However, there other evolutionary forces operating in natural populations which need to be considered to understand the evolutionary trajectories of pathogenic organisms. We are using large-scale DNA sequencing data to study the various evolutionary forces acting on *M. tuberculosis*. Our findings suggest that overall, selective constraint is greatly reduced in *M. tuberculosis*. We postulate

this is due to increased random genetic drift resulting from the serial population bottlenecks during patient-to-patient transmission. We propose a model in which genetic drift contributes to the emergence of drug resistance in *M. tuberculosis* by allowing fitness-costly drug resistance-conferring mutations to persist in absence of drug pressure.

Immunological correlates of tuberculosis infection

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Given our inability directly to detect dormant bacilli in latently infected humans, our only window into latent infection is the host response to infection. Historically, latent infection was defined as the presence of an in vivo delayed type hypersensitivity response to intradermal tuberculin PPD and correlation of skin test responses with clinical outcomes in tuberculosis-exposed populations formed the foundations of our understanding of latent infection. Over the last decade, the advent of a more specific, sensitive and dynamic ex vivo immunological marker of infection, the interferon-gamma release-assay (IGRA), has substantially advanced our understanding of the natural history of tuberculosis infection. More recently, T cell cytokine-profiling to quantify functional T cell subsets has recently generated important insights into the pathophysiology of chronic viral infections and is now beginning to shed new light on the host-pathogen equilibrium in tuberculosis infection. Gene-expression profiling has widened still further the range of host responses that can be measured. Collectively, these new tools for studying latent infection are transforming our understanding of latent infection into a range of distinct entities in the spectrum of the host-pathogen equilibrium and may reveal differences in the ability of drug-resistant and drug-sensitive strains to propagate and establish infection in the host. These new insights will likely facilitate development of more powerful prognostic biomarkers, new agents for drug-resistant tuberculosis and identification of correlates of protective immunity.

Immunological determinants of TB disease progression

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The search for biomarkers indicating the likelihood of progression is yielding variable results. I suggest that this is because the reasons for progression are not the same in all environments. In developing countries most individuals have immune responses to *Mycobacterium tuberculosis* derived from contact with environmental mycobacteria or with *M. tuberculosis* itself. This provides partial immunity that can often protect from low dose challenge, but not from the repeated high dose challenge that occurs in poverty and crowded living conditions. BCG may provide similar partial immunity, as seen in the people in India who were mycobacterially naïve at entry into the trial (Indian J Med Res (1999) 110:56–69). In rich countries, where most challenge doses are low, immunity to low dose challenge provided by BCG is often sufficient to manifest itself as protective efficacy in clinical trials.

Animal models illustrate the differing consequences of low dose (100–200 CFU) versus high dose ($\sim 10^5$) challenge. The Th1-induced plateau in CFU seen at 3 weeks in SPF mice following low dose challenge might be a model of one form of latent human TB. By contrast, when mice are challenged with $>10^5$ organisms (into the lungs or i.v.) a temporary plateau at 3 weeks is followed by further bacterial proliferation that is partly dependent upon Th2 cytokines. This might represent a model of the human disease following high dose challenge in developing countries where TB cases with the highest levels of IL-4 and TGF-β are seen. These mediators compromise cytotoxic T cells, autophagy and apoptosis. In developing countries other factors such as malnutrition, smoking, poverty and stress contribute to this cytokine pattern. In conclusion, both in man and mouse, TB caused by high dose challenge of partially immune individuals in developing countries is immunologically different from sporadic TB following low dose challenge in the immunologically naïve. Different biomarkers, genes and mechanisms might be involved.

TB infection and disease in the naturally infected guinea pig model

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Guinea pigs have long been used as an animal model to study tuberculosis pathogenesis. They are considered highly susceptible to infection with *M. tuberculosis*, and once infected with even as little as 1–2 colony forming units of a virulent strain of *M. tuberculosis*, they develop progressive disease over a period of several months. Guinea pigs serve well as 'living air samplers' of airborne *M. tuberculosis* because of their high susceptibility and their ability to be infected through the airborne route. These characteristics also make them an ideal model system in which to study the factors that influence tuberculosis transmission and microbial virulence. The Wells-Riley studies of the 1950s, in which hundreds of sentinel guinea pigs were naturally exposed to airborne *M. tuberculosis* aerosols generated by patients residing on an inpatient ward, were instrumental in demonstrating that TB was an airborne disease. In this presentation, the speaker will discuss the observations and results of similar, but more recent, natural infection experiments

in which sentinel guinea pigs were exposed to the aerosols generated by MDR-TB patients. The topics to be covered will include a discussion of the natural infection model, the extent of infection among guinea pigs, the relatively low rate of disease progression among infected animals exposed to MDR-TB, and the implications of these observations on our understanding of MDR-*M. tuberculosis* transmission, virulence, and pathogenesis under natural exposure conditions.

Does TB latency exist?

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Individuals who harbor *Mycobacterium tuberculosis* organisms in some sort of latent or dormant state are at risk of developing active disease at some later point, and this risk is dramatically amplified by co-infection with the HIV virus. Classically, reactivation of disease as a result of re-growth of the infection has been studied in various animal models, but in the current day and age relapse of infection after chemotherapy is by far the more important issue, as is re-infection of individuals in high endemic areas who had strong resistance to the primary infection. Logically, such people should have developed strong memory immunity to the initial infections, and should therefore have a much higher level of acquired specific immunity to subsequent exposure, but the clinical data now available suggests the reverse is happening. In addition, the concept that the bacillus is somehow 'asleep' in latency may be far from the actual reality, and I will present data here showing that bacteria that persist after chemotherapy are not drug resistant, but instead have adapted physiologically by forming small biofilm-like clusters in residual lung necrosis. These bacilli are not dormant, but actively accumulating ferric iron and generating energy. These findings have various implications, including the tactics needed to develop new drugs to destroy these persisting bacteria, tactics which in my opinion are currently completely wrong.

HIV CONTROVERSIES

Pro

L Corbett. London School of Hygiene & Tropical Medicine, and Malawi-Liverpool Wellcome Trust Clinical Research Programme, Blantyre 3, Malawi

How, not if.

My argument, that self-testing can and should be made available to high risk populations, follows piloting of an oral HIV test kit (OraQuick ADVANCE HIV1/2) in Blantyre, Malawi, using a mixed-methods study to explore feasibility, accuracy and acceptability of self-testing, and to identify current gaps in the options for HIV testing and counseling. With the ac-

curacy of self-test-self-read oral tests being >99% following brief demonstration, and certain key target groups (men, couples, those previously tested HIV-negative) expressing a strong preference for self-testing options, urban Africans appear to be more than ready for self-testing. 92% of participants offered the option of self-testing did so, despite being required to undergo subsequent standard VCT: 100% would recommend self-testing to friends and family. Most found the experience liberating and empowering. Key questions remain around delivery and storage of kits, linkage into counselling, confirmatory testing, and care for those who test positive, and quality assurance.

Con

F Salaniponi. KNCV Tuberculosis Foundation, Nairobi, Kenya

Settings: Various discussions on the debate surrounding HIV controversies regarding 'Walk in TB testing and self testing for HIV'.
Objective: A debate opting against 'Walk in TB testing and self testing for HIV'.
Design: A systematic summary of literature on HIV controversies, looking at among many things, the thematic analysis of opt-out HIV testing linked to its subsequent social behavioral dimension, social psychological, legal and ethical implications, stigma and discrimination and implications for public health.
Results: Literature review unveils a substantial distressing psychological reaction that HIV positive test individuals go through characterized by traumatic events and theories, negative valiance, lack of controllability and sadness. It further compounds that knowing one's HIV infection can be stressful and frightening. Where resources are generally inadequate to support HIV testing and linkage to care, and increasing stigma and discrimination, in the current concept of 'rethinking rights and responsibilities in a time of AIDS'. Testing and HIV notification are likely to push the disease deeper underground. It is not beneficial to promote the concept of 'walk in TB testing and self testing for HIV'.

Treating the HIV-infected TB patient in the same clinic

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Tuberculosis and HIV co infection has emerged as a major global public health and clinical challenge. The biologic, epidemiologic, and clinical interactions between drug susceptible and drug resistant tuberculosis and HIV require increasing collaboration between programs and integration of services to achieve the goals of reducing incidence and prevalence and decreasing morbidity and mortality from both diseases. Programmatic and resource barriers blunt these goals

and include limited national program communication and separate funding streams, staff and facilities. In addition, clinical barriers include continued concerns about additive toxicities, drug-drug interactions, pill burden and IRIS. Finally, TB and HIV have developed differing traditions and cultures of individual patient and public health approaches which limit integration. All of these can be addressed and overcome and lessons learned from each can inform and improve the other. Recent examples clearly demonstrate that a strategy of integration can be successful for co-infected patients with both drug susceptible and drug resistant TB and HIV. Examples of these will be examined. Broad program principles and minimal standards of TB-HIV service integration are essential but program designs and components may vary by country and even within countries, as a result of differing TB and HIV prevalences, resources, levels of expertise, and program settings. Nevertheless, although not without challenges, from the broad programmatic view and especially from that of the individual patient with both diseases, TB and HIV integration, with co-location of services treating the HIV-infected TB patient in the same clinic and community setting, improves access and diagnosis, enhances treatment adherence, reduces loss to follow-up and assures better outcomes. Defining of the appropriate levels of integration and their respective benefits in different settings requires further operational and implementation study.

Walk-in TB testing and self-testing for HIV

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Problem: Despite significant global efforts case finding for tuberculosis is failing to meet the 70% target set by the Stop TB partnership. Combined activities against TB and HIV are increasing globally but still only 22% of TB patients knew their HIV status in 2008. Unless case detection of both TB and HIV increase, control of these two diseases will not be achieved.
Discussion: This presentation will discuss the options for increasing case detection of TB and HIV by offering walk-in testing for TB and HIV and will discuss opportunities to further increase the uptake of HIV testing by offering self-testing. The presentation will also discuss the risks and benefits of such strategies for the individual and also the communities in which they live.

INNOVATIVE ADVOCACY, COMMUNICATION AND SOCIAL MOBILISATION TO ADDRESS TB AND TB-HIV CHALLENGES

Voices and images of persons affected by TB: the use of the Photovoice method for social change

R Lacson, R Orduño. TB Photovoice, Seattle, WA, USA

From 2005–2007, Photovoice, a community-based participatory research method developed by Dr. Caroline Wang, was used to focus on the agency of individuals affected by tuberculosis from South Carolina, the US-Mexico Border, Brazil and Thailand. This initiative, referred to as TB PhotoVoice (TBPV), was qualitatively assessed for fidelity to the original Photovoice model and for impact on participants from the four sites. The critical reflections of our TBPV field experiences will contribute to bridging the gaps between research, policy-making and practice. By examining: 1) the historical, political economy of community mobilization approaches used in tuberculosis and; 2) how TB affected individuals are created as objects of knowledge, we will outline critical perspectives to address the ethical responsibilities to affected communities not traditionally involved in health policy making, and to examine the struggles to maintain the integrity of Photovoice. Since 2007, other TBPV sites have expanded into other regions of Mexico, the Philippines and South Africa with varying human and material resources as well as technical assistance. As more community mobilization approaches are promoted and supported in other parts of the world, we have a responsibility to share the critical frameworks used to evaluate these experiences in order to illuminate the ways in which people are challenging the silencing of TB patients and are attempting to structure a more equitable participation of persons affected by TB in civil society and global TB discourse.

Collaborative activities for integration of TB-HIV services: Nigeria, Rwanda and Zambia

E McEwan. Catholic Relief Services, Baltimore, MD, USA

Background: Tuberculosis and Human Immunodeficiency Virus (HIV) are life threatening illnesses individually, but become more severe when people are co-infected. An important key to fighting co-infection lies in the integration of services.
Objective: Provide community volunteers and Local Partner Treatment Facility staff with resources to screen for TB among HIV+ clients.
Design and methods: In Nigeria and Zambia, the CRS-led AIDSRelief consortium established TB screening sites, supporting them with quality assurance, laboratory upgrades, training in smearing techniques,

counseling and testing with emphasis on TB-HIV co-infection management. In Rwanda and Zambia, trained community volunteers screened HIV+ clients using translated versions of the WHO's TB screening checklist, referred TB symptomatic to MoH centers, and provided messages on the relationship between TB and HIV.

Results: Since 2004, AIDSRelief in Nigeria has screened 47% of HIV+ clients for signs of TB, 94% received follow-up laboratory screening, and based on clinical or laboratory diagnosis, 17% of those diagnosed with active TB began treatment. In Zambia, 680 HIV+ clients with active TB, based on clinical or laboratory diagnosis received TB treatment. In Rwanda, 84% of HIV+ clients were screened for TB, and based on clinical or laboratory diagnosis, 25% began treatment.

Conclusion: Integration of HIV and TB services is essential to ensure timely diagnosis and treatment to HIV+ and TB clients. Trained community-based groups are key stakeholders in screening for active TB among HIV+ clients and making prompt referrals to life-saving treatment.

'A Better Picture': creating innovative ACSM campaigns and strategically engaging audiences

D Schumann. Damien Schumann Photography, Cape Town, Western Cape, South Africa

Setting: Examples from South Africa and Mexico.

Objective: To inspire critical and innovative thinking when creating ACSM campaigns to assure maximum results.

Design: Emphasis will be placed on the structuring, market research and interpretation, execution, and lessons learnt from campaigns that have made a difference. Using exhibitions with a specific focus in TB and related matters like co-infection and stigma, such as The Shack (a successful Advocacy tool), Dialogues (a social mobilization tool within areas of high TB-HIV prevalence) and Face It—The Stigma Exhibition (used for communications), Schumann will explain how these campaigns were designed to reach their specific audience, the structures that were required to make these possible, what worked and share suggestions on what can be innovated upon.

Conclusion: By the end of this symposium we aim to have shared a refreshing and dynamic approach to ACSM. More than offering a single solution we want to generate a lateral form of thinking that can be shaped to suit any situation. This will maintain a consistent development to keep up with changing conditions, social dynamics and requirements in engaging audiences.

'Nuestra Casa': achievements and lessons learnt in conducting an innovative ACSM strategy

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Nuestra Casa (Our Home, in Spanish) is a touring project for tuberculosis (TB) Advocacy, Communication and Social Mobilization (ACMS). Nuestra Casa is a three-dimensional house that reflects the life and stories of people affected by TB (PATB) on the U.S.-Mexico border. It is a tool that promotes awareness among decision makers, health providers, and the public to get involved in concrete action to prevent the spread of TB, reducing the suffering, the number of cases and deaths caused by it. This project stems from the need to reinforce ACMS in Mexico. Realizing that the community of persons affected by TB must be involved and their real-life situations addressed if efforts to combat the disease are to be effective. Project Concern International and the Alliance of Border Collaboratives in partnership with Mexico's National TB Program, with financial support from the U.S. Agency on International Development, adapted the concept of 'The Shack' developed in South Africa by Damien Schumann. Nuestra Casa is a Mexican adaptation and is intended to provide a new perspective on the TB problem, increasing political will to improve prevention and control and mitigate stigma and discrimination experienced by the persons affected by TB. It consists of a living room, kitchen, bathroom and a hallway or 'Corridor of Hope,' a small patio with a clothes line for pubic comments. Nuestra Casa became a vehicle for the presentation of the Voices and Images of TB (Photovoice) exhibition. Local community and social research programs around Mexico have exhibited Nuestra Casa. More than 10,000 visitors have seen the exhibition. Nuestra Casa became an international phenomenon at the 40th Union Conference on TB in Mexico. It is on exhibition at the Centers for Disease Control and Prevention. Lessons learned, personal testimonies, photographs, examples of community participation and involvement of PATB, as well as the impacts of the exhibit will be presented.

Building partnerships to bring NGOs on board and harness their contribution to TB control

T Dlamini. NTP Ministry of Health, Mbabane, Swaziland

Swaziland is a small landlocked country situated between South Africa and Mozambique covering an area of 17 364 km². The country has a predominantly (77%) rural population of about 1.1 million (2006 Census) people. Swaziland is currently facing a severe and unprecedented TB, TB-HIV and MDR-TB situation. The country has consistently had the highest estimated TB incidence per capita (1198/100 000 popu-

lation) in the world (WHO 2009). This is in addition to having one of the highest HIV prevalence rate of 26% in the general population (SNAP 2009, UN-AIDS 2009). An estimated 30% of Swazi TB patients receive health care services through CBOs, FBOs and NGOs. The national TB programme strategy to harness the resources and competencies of these organizations in a way that ensures synergy and complementarity in their operations. This initiative also aims to improve geographical and economic access to quality TB diagnosis, treatment care and support as well as empowerment of the community through intensified health promotion interventions. The Swaziland NTCP initiated a partnering process to harness the resources and competencies of these local actors to achieve this objective. This led to the formation of the Swaziland Stop TB Partnership which was launched officially on 24 March 2009. This presentation outlines the current status of the partnering process, the achievements so far and the future direction of the Swaziland Stop TB Partnership.

COPD IN LOW- AND MIDDLE-INCOME COUNTRIES (LMICS)

What we know and don't know about COPD in LMICs

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COPD is defined as obstruction of the airway that does not respond to bronchodilators. Operationally it is defined as an abnormal ratio of FEV1/FVC on spirometry. It is strongly associated with cigarette smoking and old age. The global burden of disease programme has predicted a major increase in COPD in low and middle income countries due to the demographic transition to an older age profile in these countries and to the increased prevalence of smoking. Because of a lack of spirometric data from low and middle income countries, the current situation is, however, poorly understood. Some research has started to throw some light on the problems. Although historically smoking levels have been low particularly among women in some low income countries, there are other risk factors that may be more serious. Indoor air pollution may be very intense for some women, in particular, and for their infants. There is also concern that many of the 'dirty' industries that are now part of the West's industrial history are still largely unregulated in other parts of the world. Other potentially important issues in low income countries are the extent of childhood infections and the prevalence of pulmonary tuberculosis. It is well established that the severity of COPD is linked to the absolute size of the lungs. Current evidence is that this is much lower in countries with GNP/per capita of less than about

$11,000. For a similar prevalence of disease these countries are likely to have much worse outcomes. The primary response to this coming epidemic has to be through primary prevention, but secondary prevention strategies need also to be identified and tested. Little is known of their effectiveness. Treatment is largely symptomatic with aggressive management of exacerbations. There is little evidence that the low income countries have systematically ensured availability and efficient use of resources for such management.

The relationship between tuberculosis and COPD in LMICs

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COPD is predicted to become the third largest cause of death by the year 2020. The prevalence of tuberculosis is high and even rising in some LMICs. The aim of this study is to assess the association of tuberculosis disease as a risk factor for COPD, within the context of the Burden of Obstructive Lung Disease (BOLD) study. Population-based samples aged $\geqslant$40 years from 14 countries ($n = 10\,712$) answered a respiratory questionnaire and performed spirometry using standardised methods. Multiple logistic regression was used to estimate the effect of a history of doctor-diagnosed tuberculosis disease on COPD. To assess the strength and consistency of the association with tuberculosis, random effects meta-analysis was undertaken. Population attributable risks (PAR) were estimated for each sample. A significant association of tuberculosis with COPD was observed (pooled OR for all sites 1.78; 95%CI 1.17–2.72). LMIC sites from South Africa (OR 3.14; 95%CI 1.96–5.02) showed a significant positive association, and Philippines (OR 2.23; 95%CI 0.94–5.29) had a positive association which was of borderline significance. There were small numbers of persons with both tuberculosis and COPD at all the other sites. However, 10 sites had positive odds ratios. Tuberculosis was estimated to account for a 16% of COPD in South Africa, and 9% (95%—1–18) in the Philippines, although the latter was not statistically significant (PARs). Tuberculosis is associated with COPD in LMICs and this has implications for public health agendas in order to prevent morbidity and mortality from both these common diseases.

TRANSLATING ASSESSMENTS INTO TRAINING AND EDUCATION INTERVENTIONS FOR TB AND HIV PROGRAMMES

Evaluation of an international training course to build programmatic capacity for tuberculosis control

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Background: The international training course on tuberculosis management at the Research Institute of Tuberculosis (RIT), Japan, has been conducted for the past 47 years for intermediate level health staff. As the outputs of the course, all of the participants have been requested to develop and submit an Action Plan Project (APP) report or an Operational Research Project (ORP) report by the end of the course.

Objectives: To assess the outcome of the international training courses on tuberculosis conducted at RIT.

Methods: Target population of this study was all participants who attended the training courses for intermediate level medical officers at RIT from 2001 to 2007 and whose e-mail addresses were available. Survey period was from September to December 2008. Structured questionnaire forms were sent off electronically by e-mail as attached files.

Results: Among 93 ex-participants whose e-mail addresses were available, 62 responded (67%). Among them 34 were those who had submitted APP reports and 28 who had submitted ORP reports. Among 34 with APP reports, 27 (79%) started APP activities, and 24 of them accomplished more than half of the activities planned. Among 28 with ORP reports, only 11 (39%) started ORPs. Among them, 10 (36%) collected data and 7 (25%) analyzed them. Only one ex-participant wrote a draft paper as of the survey period. The reasons why some could not start ORPs were lack of funding, having no time allocation to do it, disapproval from supervisors, and people moved out of TB control.

Conclusion: Majority of the ex-participants with APPs has started and accomplished the planned activities well. However, less than 40% of those with ORPs has started ORPs and analyzed data. Backup of funding, enough time allocation, permission of the supervisors are pre-requisite to conduct ORPs. Regular monitoring measures as one of the follow-up mechanism of international training course may be needed.

Facility-based infection control trainings in Mexico

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Setting: Mexico's National Tuberculosis Program (NTP): three state programs (Chiapas, Chihuahua and Jalisco) and six facilities, two in each state.

Objective: To build capacity within Mexico to ensure effective infection control measures and to strengthen the National TB Infection Control Plan (NTICP).

Design: An existing training curriculum, tested throughout Latin America and designed to develop local capacity, was adapted to meet the needs of the Mexico NTP; the needs were identified previously by a needs assessment exercise. The implementation of the curriculum involved not only training of participants, but also assessments of the facilities.

Results: A total of 146 participants were trained in three different states. To this date, the Tuberculosis Infection Control (TBIC) institutional plans have been developed for five out of the six participating facilities. Participants have reported high levels of satisfaction with program activities and materials. The average TBIC knowledge of participants has increased significantly. One webinar and one conference call have been conducted as follow-up activities. Additionally, five participants have been trained as facilitators. The evaluation results have been used to improve activities and materials.

Conclusions: This intervention has led to rapid, inexpensive changes in practice at the participating facilities. Furthermore, institutional administrators' and TB program officials' commitment to the concepts of TBIC appears to be enhanced, and this will be a significant factor in overcoming barriers for the implementation of TBIC plans. The Mexico NTP has acquired the knowledge, tools and materials needed to strengthen their NTICP, and in the process has built a strong team committed to its successful implementation. However, stakeholders recognize that to achieve and maintain this objective further technical assistance and ongoing monitoring and evaluation will be necessary.

Developing and implementing a competency-based training for district level managers in TB control

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Background: Tuberculosis has remained a public health challenge in Kenya. TB services are integrated into the general health care system with District TB/Leprosy coordinators (DTLCs) and District medical laboratory technologist (DMLTs) being the backbone of the TB program implementation at the district. Human resource related issues poses key challenges

in TB control with some district coordinators demonstrating inadequate managerial competencies.

Setting: National Tuberculosis Control Program, Kenya.

Objective: Develop a training curriculum with relevant stakeholders to address core competency-based training for district level managers in TB control in Kenya.

Design: A structured process of training was deployed. Follow-up of the trainees was designed and checklist developed.

Results: Using the developed curriculum, first training lasting three weeks was done in November 2009 and twenty three DTLCs and DMLTs participated. A scheduled Follow-up of the trainees at their working place was done in March 2010 and both the trainers and the trainees' supervisors participated. The follow up visits gave input on: the effect of the Management course on the trainees, their supervision and ways to improve the Management course. Overall, the trainees demonstrated significant improvement in their performance as district TB managers.

Conclusion: An in-country competence based 'Management Course for Mid-level TB managers' is realistic using available resources including homegrown experiences.

TREAT TB: INNOVATIONS IN RESEARCH

The TREAT TB Initiative: an overview

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Setting: Global, regional and national tuberculosis control activities.

Objective: To address gaps in programmatically-relevant research to improve tuberculosis control policy and practice.

Design: TREAT TB is supported by a five year USAID Cooperative Agreement that commenced in October 2008. Through TREAT TB, The Union has built a research partnership model that has every potential to stimulate changes in international standards and practice.

Results: TREAT TB has charted an initial path to contribute to new knowledge through a diagnostic tools initiative, clinical trials and other research of priority patient management questions, and targeted country-level operational research. The diagnostic tools initiative has moved forward on key systematic reviews, development of a novel approach to evaluate new diagnostic tools and conception of a model to assess the needs and impact of new diagnostic tools on a larger scale. Patient management research activities to date include global consultations on key unresolved research areas and protocol development and site preparation for a clinical trial on a shortened, stan-

dardized regimen for MDR-TB. Country-level operational research support has resulted in study implementation in Malawi and South Africa—the latter part of a comprehensive country-level operational assistance program.

Conclusion: TREAT TB has, and continues to identify key gaps in global research activities in tuberculosis control. Through direct support, as well as leveraging of other resources, TREAT TB will ensure that these gaps are addressed and research is undertaken that is most relevant to program needs with the potential to impact policy at all levels.

The TREAT TB diagnostic tools initiative: systematic reviews, field evaluations and modeling

A K Detjen. International Union Against Tuberculosis and Lung Disease, New York, NY, USA

The TREAT TB Diagnostic Tools Initiative (DTI) aims to inform national and global policies and practices by addressing gaps in the research of new TB diagnostic tools: Systematic Reviews (SR) create the evidence base for policy decisions on new diagnostic tools. Methodological approaches tend to vary across studies, complicating their systematic assessment and comparability. Operational aspects of new tools are almost equally important to diagnostic accuracy for policy decisions. In addition to diagnostic accuracy, SRs under TREAT TB address these methodological and operational challenges, identifying gaps for future research. Field Evaluations. Successful implementation of a tool depends not only on its accuracy. Implementation within health systems requires adaptation of laboratory and clinical infrastructure and algorithms. Patient's access and costs play an important role whether a new tool will affect patient outcomes. Using an impact assessment framework, suggested in the New Diagnostics Working Group's 'blueprint', TREAT TB developed a novel approach to comprehensively assess the implementation of new diagnostics. This approach will first be used to assess the implementation of Line Probe Assay in three different settings and will later be adapted to other tools. Modeling Exercises under TREAT TB addresses the needs and potential impact of new tools on a larger scale to provide improved guidance regarding the packages of diagnostic tools most suitable for different settings. Two models comprehensively gather the information needed for decision making: transmission modeling projects the impact of new tools on the transmission of TB within a population. Health systems modeling evaluates the impact of new tools on the functioning of health systems through the analysis of key operational questions and health system requirements. These three approaches are interlinked and provide essential information to improve the evidence base for new diagnostic tools for TB.

Developing country research networks

A Kritski. Rede TB, Rio de Janeiro, RJ, Brazil

Introduction: There has been a significant gap in communication and coordination between TB programmatic experts, academics, the community, and nongovernmental organizations (NGOs). In 2001, a Brazilian TB Research Network (REDE-TB) was established to bring these partners together to promote an integrated, multidisciplinary and multi-institutional strategy for TB control.

General objective: To build a successful research partnership model with potential to stimulate changes in national standards and practice to meet country needs.

Specific objectives:

Improved diagnostics: a) Improve performance of existing diagnostic tools, particularly in HIV-infected adults and children; b) Develop and evaluate the impact for the public and private sectors of the health system of incorporating new tools to detect DS-TB, DR-TB, and latent M.tb infection.

Improved treatment: a) Develop new highly potent TB drugs; b) Evaluate novel drug regimens that will shorten treatment duration and, treat patients with drug resistant TB; c) Develop capacity to perform clinical trials to build a convincing evidence base for the efficacy and effectiveness of new TB treatment regimens, respectively, through exploratory and pragmatic trials; g) Identify and validate biomarkers for monitoring TB disease activity, cure and relapse to act as surrogate endpoints for shortening clinical trials.

Improved prevention: a) Identify and evaluate the performance of optimal pragmatic infection control strategies and of new regimens; b) involve the civil society through social mobilization.

Conclusions: REDE TB has established with the Ministry of Health, the Brazilian Partnership Against TB and international organizations a solid collaboration and has helped to foster Brazilian leadership and skill in the development of a National framework for impact assessment of efficacy, equity, health system, scale-up and policy aspects regarding the implementation of new technologies in TB control.

COMBATING HIV-TB AMONG VULNERABLE POPULATIONS IN EASTERN EUROPE

Northern Dimension cross-border cooperation in combating HIV and HIV-TB

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The Northern Dimension Partnership in Public Health and Social Well-being (NDPHS) was established in 2003 by thirteen governments, the European Commission and eight international organizations. The priorities of the Partnership are: 1) to reduce major communicable diseases and prevent life-style related non-communicable diseases and 2) to enhance social well-being and promote socially rewarding lifestyles. The practical work under the Partnership is implemented through Expert Groups and Task Groups. The main focus of activities of HIV/AIDS and Associated Infections Expert Group under the NDPHS lies in the prevention of HIV within the region with special emphasis on the countries/regions with particularly high prevalence and incidence. The activities include prevention of tuberculosis and other infections that are linked with HIV through social and health risk factors, pathogenesis and epidemiology. Priority areas include prevention of HIV-TB co-infections, prevention of HIV among drug users and other vulnerable populations, enhancing cross-border activities and integration of social and health care for HIV-infected individuals. Series of projects have been and are being implemented under the umbrella of the Expert Group. Low threshold service centres to prevent HIV and other infections among drug users have been established in Murmansk (in 2005) and Kandalaksha (in 2007). A new project has been started to enhance similar activities in the Leningrad Region. Low threshold approach in providing medical and social support for drug users has proven to be efficient, and has become even more actual due to the co-infection of HIV and TB. A new tuberculosis programme including component of HIV-TB co-infection is under development in the framework of the Barents Euro-Arctic Council, Working Group on Health and Related Social Issues, in collaboration with the NDPHS. This programme is expected to guide regional collaboration over many years to come.

Challenges in integrated HIV-TB prevention and care in prisons in Eastern Europe

Z Tsereteli. NDPHS, Tallinn, Estonia

More than 600 000 people are incarcerated in the prisons of the 27 European Member States on a given day, with an estimated annual turnover of 860 000 to one million prisoners. If we look to the first three countries in the list of prisoners per 100 000 population in Europe we will see that those are countries from Eastern europe: Russian Federation (608.6), Ukraine (355.3) and Estonia (311.6). Prisons are a setting in which members of most-vulnerable-groups (IDUs, migrants, ethnic minorities) are overrepresented and are living mostly in overcrowded premises under poor hygienic conditions. All these factors directly contribute to HIV and TB transmission. For every person in prison on any given day, four to six more will pass through the system that year. Released prisoners, as well as prison staff and visitors can, in a

sense, bring the prison home. That is why control of TB and HIV inside prisons is so critical for TB and HIV control in the general population. The challenges involved in integrating HIV-TB prevention and care in Prison settings include, but are not limited to, the following: lack of political leadership to ensure that prison health is a part of public health, and that serving prisoners means serving the needs of the population. Resistance to integration from the historically vertical and rather isolated TB and HIV control programmes. Financial and managerial separation of the prison health system from the rest of the health system which leads to frequent problems with procurement and distribution of drugs for both diseases. Limited knowledge and experience of prison health staff in the practical approaches to diagnostic and therapeutic issues in the TB-HIV co-infected patient. Absence of the two key prevention strategies, while tackling HIV/AIDS among the IDUs, that have been proven successful in the community.

QUALITY LABORATORY MANAGEMENT: THE SOLUTION TO PROVIDING RELIABLE LABORATORY SERVICES

Innovative approach using Geographic Information Systems for management of TB laboratory networks

M Joloba, K Musisi, D Nadunga. National Tuberculosis Reference Laboratory, Kampala, Uganda

Setting: The National Tuberculosis Reference Laboratory (NTRL), Kampala, Uganda that has a laboratory network of over 800 laboratories country wide and an established External Quality Assessment (EQA) program.
Objective: To improve monitoring, planning, interventions and advocacy for laboratory services such as EQA, specimen referral to detect MDR cases, equipment and staff training using Geographic Information Systems (GIS).
Design: Health Center III & IV, clinics and hospitals both government and non government aided involved in TB diagnosis and treatment were mapped. During the mapping exercise, the health facility laboratory was the main focus and the entrance to the laboratory was the position chosen to collect coordinates.
Results: Out of the 840 Health Facility laboratories on the EQA Program and the TB Specimen Referral System, we have been able to map 648 laboratories (77%) and 20 Post Offices. GIS has helped NTRL visually appreciate the distribution of the TB laboratories in the network in relation to workload, population structure, distances, performance and various needs. As a result, the NTRL has been able to improve planning and budgeting for its EQA, training, equipment

needs and supervision activities in the lab network. With GIS and help of data collected from the TB Specimen Referral System, it was easy to visualize the distribution of detected MDR-TB cases in the country. This aided the National Tuberculosis and Leprosy Program plan and make strategies on how to lobby for second-line TB drugs. Perhaps the biggest advantage for GIS in the laboratory network is advocacy. GIS has made it easy to summarise and convey messages about the network to various audiences such as the programme, politicians, partners, review missions and trainees. This work has been made possible with the help of several partners and these include BD, PEPFAR, CDC and Royal Tropical Institute.
Conclusion: GIS has been a helpful visual and analytical tool in managing, planning, interventions and advocacy for laboratory services.

Referral and reporting systems: optimising the flow of specimens and information and clinical impact

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Having a reliable laboratory service with good referral and reporting systems is pivotal to all aspects of health care including management of tuberculosis. This is even more critical for HIV-infected TB patients because of differences in the clinical analysis and more rapid course of the disease. Delays in laboratory confirmation of TB in relation to sample referral and reporting of results can lead to delays in initiation of therapy, prolonged infectiousness, inappropriate therapy, and missed opportunities to prevent transmission. For proper diagnosis of tuberculosis, collection of a proper sample and timely transport to the laboratory along with the essential patient information is most important. In resource limited settings with widely distributed populations, there is a need for greater resources to establish a strong and functional network of laboratory services, both public and private, and to ensure an appropriate referral mechanism with prompt and safe transport and processing of specimens. After examination, the results have to reach the clinician without any delay for proper case management. An efficient and improved communication between laboratories and clinicians is also extremely essential in this regard. Therefore, a proper system should be in place to speed up the flow of specimens and information and delivery of results, thereby improving the overall control programme.

Laboratory information systems are an indispensible tool for measuring laboratory performance

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The laboratory is a fundamental component of tuberculosis (TB) control, providing testing for diagnosis, treatment monitoring, and surveillance at each level of the healthcare system. An internet-based laboratory information management system (LIMS) could facilitate the real-time observation of case order, specimen collection, transportation, succession diagnosis procedure, reporting, and case-registry. In Taiwan, the TB LIMS was integrated in 2002 into an internet-based National Surveillance Network of Communicable Diseases (NSNCD) of Taiwan Centers for Disease Control (TCDC) with a single entryway and enhanced capability and flexibility. Each patient is given a set of barcode labels or unique identification numbers for his/her specimens. Patient's information and laboratory results are each entered at site and online transmitted to the NSNCD website. Information has been viewed online by healthcare and public health personnel with access permission. Centralized monitoring of laboratory quality index, logistics, their results and effectiveness of the service is conducted by TCDC. Outcomes are feed back to local public health department or bureau periodically. However, difficulties encountered include accuracy and timeliness of data entry, and interface of diverse information systems used in different clinical settings. Nevertheless, a well-managed LIMS can dramatically reduce the delay of the laboratory services for patient care and case management.

Laboratory accreditation as part of the solution to strengthen diagnostic services

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Accurate and reliable TB laboratory testing is essential for clinicians and health care providers to make accurate diagnoses, formulate treatment plans, and subsequently monitor the patient's response to treatment. To ensure the quality of TB laboratory services, laboratories should strive to implement a quality laboratory management system that emphasizes compliance with laboratory standards. Benefits of such a system includes 1) ensuring the quality of overall process, 2) detecting and reducing errors, 3) improving consistency within and between laboratories, 4) containing costs, and 5) recognizing the quality and reliability of work which lends credibility to laboratory results and can improve staff morale and enrichment. Accreditation is a process which gives formal recognition that a laboratory meets testing standards and provides quality services. Striving to obtain accreditation strengthens diagnostic services because it promotes implementation and compliance with standards. For TB laboratories two types of accreditation may be needed: 1) accreditation that TB laboratories meet requirements that specifically target the operation of AFB-smear microscopy laboratories, culture laboratories, drug-susceptibility testing laboratories, molecular biology testing laboratories, and TB reference laboratories and 2) accreditation that TB laboratory networks meet requirements that specifically target the performance of laboratory networks in terms of external quality assurance, specimen transport, and data management. A Union working group is partnering with the Global Laboratory Initiative of the Stop TB Partnership and representatives of other accreditation groups to develop consensus standards and accreditation schemes to meet the needs of TB laboratories.

FLUOROQUINOLONES: FRIEND OR FOE?

Fluoroquinolone resistance: a problem for the developing world?

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Fluoroquinolones are widely used to treat non-tuberculous infections such as pneumonia, urinary tract infections, osteomyelitis, and sexually transmitted diseases. Fluoroquinolone mono-therapy may be prescribed to persons with tuberculosis in whom the diagnosis is not suspected. Fluoroquinolone exposure prior to tuberculosis diagnosis is indeed common, and can result in delays in diagnosis and fluoroquinolone-resistant disease. This problem is exacerbated in developing countries, where fluoroquinolones are available over-the-counter without a prescription, and tuberculosis prevalence is high. Fluoroquinolone resistance rates in *M. tuberculosis* in developing world settings will be reviewed, along with limitations of the current data. The issue of fluoroquinolone resistance testing in *M. tuberculosis* and standardization will also be discussed.

GETTING THE AIR CLEAN: INDOOR AIR POLLUTION AND LUNG HEALTH

Strategy to reduce harmful effects of indoor air pollution

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The first step is to decide how big the problem should be before you start to undertake actions to correct it. If and when it is decided that something needs to be done, there are four components that should be addressed to reduce the problem:

1 Make available alternate, cleaner types of fuel that produce less harmful smoke;

2   Improve access to better stoves used for cooking and heating;

3   Improve the quality of the ventilation used for the stoves and

4   Provide education for behaviour change.

In order to improve the situation, the various options, in terms of risk, must be understood. The most dangerous types of fuel, in descending order, are biomass, coal/charcoal, liquid fuel and electricity. Risk can be reduced by selecting a less hazardous type of fuel. The most dangerous type of stove, in descending order, is the open fire, the surrounded fire, the improved single pot stove and the griddle stove. The worst ventilation results from having the fire in the room in which people live, having an open fire, having a hood that directs the smoke away or, finally, having a chimney on the stove, provided it is regularly cleaned. One of the most effective ways to introduce changes to traditional practices is to start where the problem is worst and people can assess the results of not doing anything. In many communities, families with children who develop pneumonia may be willing to change, especially if this entails repeated episodes of pneumonia or if several children in the family have pneumonia. These families can quickly appreciate that smoke exposure is a problem for their children. If improvement in their children's health occurs when steps are taken to reduce the smoke exposure, these families become potent and persuasive examples for changing patterns of cooking or heating in their communities.

CRITICAL ISSUES IN TB CLINICAL TRIALS

Ethical challenges in TB trials: making new drugs available

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At the present time, 6 new antituberculosis agents are in clinical trials. These agents represent four new drug classes, offering hope that completely new regimens may become possible. Such new regimens could greatly improve the treatment of patients with both drug-susceptible and MDR-TB. However, to realize this promise requires that the new agents are not introduced in a haphazard way, such that sequential drug resistance is generated. At the same time, access to such agents needs to be provided to patients who have no other treatment options. Initial access to new antimicrobial agents is traditionally provided through compassionate use and expanded access programs. Meeting the needs of patients while preserving the activity of the drugs is an important public health priority. This talk will examine the challenges of meeting these needs and outline potential mechanisms for addressing these challenges.

Defining endpoints in TB clinical trials

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Endpoints in TB clinical trials have changed substantially over the years. In the first British Medical Research Council streptomycin trial published in 1948, death, and radiological and clinical improvement were the primary focus of the analysis. With the advent of effective chemotherapy, death was no longer such a relevant endpoint and there was considerable emphasis on changes in general condition, weight, febrile state, raised ESR as well as radiographic change. In the 1960s, the use of bacteriological endpoints became more common and in many trial reports the changes in radiographic extent of disease and cavitation were no longer reported. Bacteriological relapse became the defining primary endpoint and is now widely accepted as such. However, bacteriology alone has its limitations. Care needs to be taken to ensure that isolated positive cultures are not wrongly classified as relapse and in a minority of situations, patients might deteriorate clinically or radiologically requiring retreatment without supporting bacteriological evidence. The situation has been further complicated by the introduction of highly sensitive liquid culture methods. Those patients who fail to complete treatment, those who default early in follow-up and those who are reinfected raise additional issues demanding of careful consideration. Precisely defining the intention to treat and per protocol populations are challenges which are of particular relevance to non-inferiority trials.

Biomarkers: potential to shorten time to new anti-infectives

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The Stop TB Partnership has claimed to half tuberculosis (TB) prevalence and mortality by 2015 as compared to 1990 and to reduce annual incidence to <1 per million by 2050. These are ambitious goals, which can only be achieved by combined efforts including introduction of novel anti-infectives and diagnostics. Thus, we urgently need to introduce, as soon as possible: (i) new vaccines that are superior to BCG with respect to efficacy and safety, and notably are protective against adult TB; (ii) new drugs that shorten treatment time and are effective against strains resistant to one or more current drugs; (iii) new diagnostics that allow reliable and fast diagnosis of TB. Clinical development of new anti-infectives in TB (vaccines and drugs) is time-consuming. Notably, vaccine trials can last a decade on their way from phase I to phase III. This, long and winding road can be shortened by the provision of biomarkers, which act as surrogates of clinical endpoint. Such biomarkers can be combined to a biosignature to objectively and reliably measure the outcome of the preventive or thera-

peutic intervention. In the case of vaccine trials, correlates of protective immunity which can predict vaccine efficacy would be extremely valuable. In the case of drug trials, correlates of treatment success (cure and risk of relapse) would be needed. Even though current biomarkers have not qualified as true correlates of success of intervention, they could already help clinical trial monitoring. Such biomarkers could come from different analyses including transcriptomics, proteomics, metabolomics, as well as from immunologic studies. We have already monitored a TB vaccine trial by gene expression profiling in addition to measurement of immune responses. Biomarkers alone can provide guidelines for the development of diagnostics with prognostic value that can predict outbreak of active TB in latently infected individuals.

GENDER AND SECONDHAND SMOKE

Women and secondhand smoke in Europe

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Background: Secondhand smoke exposure is an important cause of respiratory and other health problems in adults and children around the world. There are considerable differences in women's and men's domestic and occupational lives. Thus there are likely to be important gender differences in both exposure to second-hand smoke (SHS) in public and private places, and consequent health impacts. However, little attention has been given to this issue.
Objectives: To undertake a gender-based review of the evidence on SHS, including health effects, place and levels of exposure and the impact of interventions such as smoke-free legislation in Europe, in order to inform and progress effective gender-sensitive action on this issue.
Methods: Literature review, interviews with key informants from a range of countries in Europe, an INWAT-Europe expert seminar.
Results: Limited sex disaggregated data are available on SHS in Europe. However, it is clear from available data that: SHS impacts on women's health, many women are still exposed to SHS in public places (including work) and in the home, and this varies considerably between countries. European women on average spend more time at home than men. Thus the home is particularly important both for women's exposure to SHS and for women as a source of SHS exposure for children. Many women, particularly those living in disadvantaged circumstances, face barriers and challenges in trying to protect their children from SHS exposure in the home.
Conclusions: Recommendations are made for gender-based action at European, national and local levels. These include policy makers, health professionals,

non-governmental organizations and research funding bodies.

Gender and secondhand smoke exposure in the home

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The introduction in March 2006 of legislation banning smoking in public places in Scotland raised concerns that smokers would smoke more at home and so increase the exposure of those living with them to tobacco smoke. Drawing on interviews from two qualitative studies conducted after the legislation was implemented, we use gender based analysis to explore where and why smokers, who lived with non-smokers including children, continued to smoke in their homes. Although very few people had increased their home smoking as a direct consequence of the legislation, many who already smoked there continued, and most women reported little or no disruption to their home smoking post-legislation. Also, because of the changing social environment of smoking, and other life circumstances, a minority of women had increased their levels of home smoking. Although home smoking was linked to gendered caring responsibilities, other issues associated with being a smoker also meant that many women smokers chose to keep smoking in their homes.

The health impacts of comprehensive smokefree legislation: the Scottish experience

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Introduction: A comprehensive ban on smoking in enclosed public places was implemented in Scotland in March 2006 and a complex national evaluation was developed to assess the impact of the legislation.
Method: Using a 'before and after' design, the evaluation focused on eight key outcome areas—compliance; second-hand smoke (SHS) exposure; smoking prevalence and tobacco consumption; tobacco-related morbidity and mortality; knowledge and attitudes; socio-cultural adaptation; economic impacts; and health inequalities. Assessment of each of the outcome areas was based on a combination of secondary analyses of routine datasets and the results from eight research studies.
Results: Large reductions in SHS exposure among both bar worker and the general population, have been accompanied by a dramatic 17% reduction in

hospital admissions for acute coronary syndrome; improvements in the respiratory health of bar workers; and a reduction in asthma admissions in children. Behavioural adaptations to the legislation have included a reduction in tobacco consumption and smoking prevalence and an increase in the implementation of stricter smoking restrictions in the home. We found no evidence of widening health inequalities up to one year post-legislation. However, both adults and children who live with smokers continue to be exposed to SHS at levels equivalent to occupational exposure pre-legislation.

Conclusion: Scotlands smoke-free legislation has had on the health of the Scottish population but urgent action is required to reduce SHS exposure in the home.

DEVELOPING A GLOBAL GUIDELINE FOR NUTRITIONAL SUPPORT TO IMPROVE THE HEALTH STATUS OF TB PATIENTS

The perfect diet: what's known about the micro- and macro-nutritional requirements of TB patients?

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Although malnutrition is a well known risk for developing active TB, the role of nutrition as prevention and therapy in the disease process has not been well studied. Undernutrition is both a predictor and an outcome of TB disease progression. Provision of adequate micro- and macro-nutrients supports a competent immune system, preventing the vast majority of TB-infected persons from developing active disease. Conversely, low BMI in those with TB disease are more likely to die, while low BMI in those with multidrug resistance are at increased risk of advanced disease and death. Although the ratio of female to male TB cases is 1:1.5-2, females are more likely to progress to active TB and have a higher case fatality for a variety of reasons. TB may flare during the stress and increased nutrient needs of pregnancy or due to co-existing infections like HIV, with increased risk of negative health outcomes for both mothers and their infants. Women of childbearing age may be an important target population for improving nutritional status, therefore, in order to prevent TB disease. Adequate intake of energy and protein to achieve a BMI of 18.6–25 kg/m^2 and sufficient micronutrients (vitamins A, B_6, D, C, E and selenium and zinc in particular) show promise for both prevention of TB disease and improved disease outcome. Providing a simple yet powerful boost to the immune system is needed . . . nutrient dense food! This, however, is a public health challenge throughout the world, and especially in low-income settings.

SYMPOSIA: MONDAY 15 NOVEMBER 2010

INNOVATIVE APPROACHES TO SCALE UP MDR-TB TREATMENT GLOBALLY

How is laboratory innovation assisting MDR-TB scale-up plans?

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TB laboratory plays a critical role in MDR-TB scale-up plans because these patients require TB laboratories that have both culture and drug susceptibility testing (DST) abilities, in addition to the usual AFB microscopy services. In high burden countries with most MDR-TB cases, the challenge is to rapidly scale up laboratory capacity in culture and DST to reach a level that can be useful for longer term management of MDR-TB cases that necessarily require much longer treatment duration. Innovative laboratory approaches have opened up many new possibilities that can potentially shorten time for diagnosing MDR cases, promising earlier treatment and infection control measures. The main difficulties facing high burden countries are to cope with high number of cases on one hand, and trying to figure out what could be the best laboratory technology that can be adopted for specific country situations. Examples are (1) use of Light Emitting Diode (LED) microscopy in place of traditional Ziehl Neelsen staining, and (2) molecular approaches in detection of rifampicin and isoniazid resistances. Proper laboratory setup is essential for the latter technology. Validation and evaluation of these new technologies are required to provide crucial information on performance of these newer techniques under field conditions. Upon implementation, there are further difficulties in training and retaining laboratory personnel, as well as providing career prospects. The massive human and physical resources required for programmatic management of MDR-TB has often been under-estimated by many TB programs. Innovative laboratory approaches, if properly assessed and adopted, can open new paradigms.

From project implementation to national scale up of MDR-TB: the experience from China

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Multidrug-resistant tuberculosis (MDR-TB) has become a serious threat to TB control in China. It is estimated that 12 000 new MDR cases emerge annually in China, accounting for approximately 24% of the global burden of MDR-TB. To address this challenge, China launched MDR-TB management programs in Hubei and Guangdong provinces in 2006 with the support of the Global Fund (GF) MDR-TB project, and has since scaled up the projects in the following years. By March 2010, the China GF MDR-TB project covered 41 prefectures of 12 provinces in China. Overall, 9388 MDR-TB suspects had been registered, among which 1334 MDR-TB cases were confirmed using the traditional drug susceptibility test (DST). By now, more than 700 patients have already received treatment. The China GF MDR-TB project strategy has been developed to improve case detection by incorporating high risk group screening and improve MDR-TB treatment by using standardized treatment regimen. Based on previous experiences, China has developed a national MDR-TB control model and plan. A patient-centred care model has been used to remove the barriers for case finding and promoting proper MDR-TB treatment and management at the provincial, prefecture, county and community levels. The core components of the MDR-TB control plan include the expansion of coverage and targeted groups, as well as the use of rapid diagnosis methods, standardized treatment regimens, an electronic recording and reporting system and high quality patient care. A stepwise approach is used to execute the planned implementation, and includes 4 important parts: the Central level Pilot Phase (2007–2009), the Preliminary Scale-up phase (2010–2012), the Rapid scale-up phase (2013–2017), and the Full coverage phase (2018–2020).

CLINICAL RESEARCH IN CHILD TB: AN UPDATE AND FUTURE CHALLENGES

The role of chest radiography in the diagnosis of TB and follow-up of treatment response in children

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TB is difficult to diagnose in children and 'suggestive' chest radiology has an important place in diagnostic pathway. Frontal chest radiograph, sometimes with a lateral view, is used. The benefits of additional or penetrated views are not universally accepted. Radiological manifestations can be categorized into primary and post-primary disease. Mediastinal lymphadenopathy—the radiological hallmark of primary TB—is often seen with parenchymal lesions or atelectasis. Adenopathy presents as discrete, circumscribed, dense soft tissue shadow but can also manifest as ill-defined hilar prominence, best detected on the lateral view. Over-diagnosis of hilar adenitis in slightly rotated or expiratory films or due to confounders like thymus, body of manubrium, etc. is well described; so is the large inter- and intra-observer variations. On CT Chest, a sensitive tool, involved lymph nodes appear as central areas of low attenuation with peripheral rim enhancement. CT readers have only moderate agreement on the presence of the lesion, particularly in the anterior mediastinum. CT has high risk of radiation exposure. Progressive primary TB manifests radiographically as parenchymal disease, atelectasis, or pleural effusion, or as miliary disease. Typically, a uniform homogenous parenchymal consolidation, with ill-defined borders, sometimes with an air-bronchogram is seen. It may resolve without radiological sequelae over months to years; in about 1/3 a scar persists. Lobar or segmental atelectasis due to endobronchial disease or extrinsic bronchial compression is seen frequently in children under 2 yr. Early on, lymph nodes and areas of infiltration may actually increase despite adequate therapy; due to the hypersensitivity reaction. Post primary TB results either due to reactivation or re-infection and is seen usually in adolescence or later. Distinguishing features include a predilection for the upper lobes, absence of lymphadenopathy and a propensity for cavitation.

Results from field: novel diagnostics in children

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Background: TB is difficult to detect in children living in developing countries because of lack of laboratory facilities, high prevalence of malnutrition and lack of community awareness. Facilities for detection and treatment of childhood TB in Bangladesh currently exist only in specialized, large hospitals in urban areas.
Objective: This program research aimed at establishing a system for diagnosing and treating TB among children, creating awareness, and assessing the magnitude of the problem in two rural sub-districts of Bangladesh.
Design and evaluation methods: All children 0 months to less than 15 years, living in two rural sub-districts (total population ~463 000) of Bangladesh were screened for symptoms suggestive of TB. Children

suspected to have TB, based on screening procedure, were seen by a doctor who used the WHO guidelines for diagnosis of TB. Children diagnosed to have TB were treated under DOTS. In addition to screening children, the community health workers (CHWs) arranged discussions with community groups at periodic intervals on cause, prevention, symptoms, and treatment of child TB. Sessions of folk songs focusing on childhood TB were organized in rural marketplaces for creating awareness.

Results: Out of 153 433 children screened for TB by the CHWs, 2341 were initially suspected to have TB. A re-screening of the 2341 children by the doctor resulted in 1002 children suspected to have TB. Eighty children were diagnosed to have TB and were linked to the DOTS program. All children have completed the treatment, except 3 children who are still on treatment. To increase awareness about childhood TB, 4733 courtyard meetings with household members were held. A total of 435 meetings were held in schools while 32 sessions of folk songs were organized.

Conclusions: The magnitude of childhood TB is high in Bangladesh. The disease can be diagnosed and treated at the community level provided sufficient awareness is created, and a trained doctor, facilities for chest X-ray and tuberculin skin testing are available at the sub-district level.

Biomarkers in childhood TB

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Childhood tuberculosis (TB) remains a major cause of child mortality worldwide with ca. 1 million new cases annually. Notably, children have an increased risk of rapidly progressing to active TB disease with highest risk under the age of 2 and lower risk between 5 and 10 years of age. The situation is further complicated by higher incidences of extrapulmonary TB. Childhood TB diagnosis remains insufficient and novel approaches are urgently needed, not the least because of the paucibacillary nature of infant TB, which results in a high proportion of false sputum-smear negative diagnoses. Biomarkers could facilitate design of novel diagnostics for childhood TB. These include different biomics assays (transcriptomics, proteomics and metabolomics) as well as antigen-specific immune assays. Because of the central role of T lymphocytes in host defense against TB, immune diagnosis should focus on these cells. Currently available second-generation diagnostics focus on the antigen-induced interferon-gamma (IFN-γ) secretion by T cell-based IFN-γ release assays (IGRA). Although IFN-γ is an important mediator of protective immunity in TB, it is an insufficient biomarker of protective immunity. Deeper insights into the immune response against TB in children will facilitate the development of novel immune biomarkers. These include phenotypic charac-

teristics, coexpression of multiple cytokines and expression of cytotoxic molecules. The latter comprise granulysin, perforin and granzymes. Evidence indicating that granulysin can directly attack *Mycobacterium tuberculosis* in vitro and, in combination with perforin, can also attack *M. tuberculosis* within macrophages points to this molecule as an interesting candidate biomarker. Our analyses suggest that granulysin is expressed not only by CD8 T cells, but also by CD4 T cells in children with active TB and that granulysin-expressing cells express a memory phenotype.

Results from the field. MDR-TB in children: clinical features and outcome of culture-confirmed cases

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Setting: Childhood MDR-TB is underestimated as culture and drug susceptibility testing (DST) is often not done and DST results of adult source cases are rarely taken into consideration when managing child contacts. We describe clinical and outcome data for children with culture-confirmed MDR-TB.

Methods: All children <15 years of age diagnosed with confirmed MDR-TB and managed at two referral hospitals from March 2003 to December 2008 were included in a retrospective study. Clinical and outcome data were retrieved from hospital and clinic notes.

Results: During this period 113 children, median age 50 months (range 3–180), were diagnosed; 67 (59%) were girls. In 78 (69%) a source case was identified; of these 46 (59%) had MDR-TB, 1 had INH-resistant TB, 2 drug-susceptible TB and in 29 cases the DST was unknown (9 died). Of the 113 children, 55 (49%) had previously completed TB treatment and a further 15 (13%) had previous prophylaxis—the majority of these failed first-line treatment or prophylaxis. Second-line anti-TB treatment was started in most children either according to adult source case's DST or child's isolate DST result, although 4 died before MDR-TB diagnosis, 2 were lost to follow-up, 1 was transferred out and a few children improved on first-line treatment. Pulmonary TB alone was found in 73 children (65%), extrapulmonary TB alone in 10 (9%) and both forms in 30 (26%). HIV status was known in 102 (90%); 43% were HIV-infected. Cure (81) or treatment completion (15) was achieved in 96 (85%) children, 12 (11%) died (7 HIV-infected), 3 were lost to follow-up or transferred out, and 2 XDR-TB cases failed treatment (restarted on new regimens).

Conclusions: MDR-TB diagnosis in children is often delayed despite known adult MDR-TB contact. However, high cure and treatment completion rates were achieved in this patient cohort with individualized management.

IMPROVING INTEGRATED HIV CARE AND TREATMENT SERVICES FOR PATIENTS DIAGNOSED WITH HIV IN TB CLINICS

Evaluation of providing integrated HIV care and treatment services in a TB clinic in Tanzania

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Background: Tuberculosis (TB) is the most common life-threatening disease and a leading cause of early deaths among people with HIV/AIDS, and so, integrating TB and HIV care may improve patient outcomes. Tanzania Ministry of Health data show that 41% of TB patients are HIV-infected, but only 30% of these receive antiretroviral therapy (ART) during TB treatment. In 2006, Tanzania piloted integration of HIV care into a regional TB clinic serving 36 peripheral TB clinics. TB providers assessed HIV-infected TB patients for ART eligibility and, when indicated, provided on-site ART and monitoring. This study evaluates this pilot.

Methods: Retrospective medical record review of TB patients, who were diagnosed with HIV and enrolled in the pilot between July 2006 and June 2008, was conducted. We extracted data on enrollment in HIV care, ART provision and clinical outcomes.

Results: Forty-five percent (1363 of 3029) of HIV-infected TB patients within this TB clinic network sought HIV care; 60% (821 of 1363) enrolled in the pilot program. Records were retrieved for 670 of 821 (82%) enrolled patients. 89% (596 of 670) enrolled in HIV care within one day of HIV diagnosis. 387 (81%) of 478 ART-eligible patients were started on ART, and 100% received appropriate regimens. Median time to ART start was 30 (7–213) days post-enrollment and 15 (0–168) days after ART eligibility determination. ART regimens were stopped or changed for five (1%) of the 387 patients.

Conclusions: Provision of HIV care services within a regional TB clinic resulted in early HIV care enrollment, high rates and early initiation of appropriate ART regimens for enrolled patients. Expansion of HIV care to TB clinics may offer an opportunity to improve outcomes for HIV-infected TB patients. However, further studies are needed to address the overall low uptake of HIV services and patient perspective on integrated model.

M. TUBERCULOSIS STRAIN DIVERSITY IN HIGH-BURDEN COUNTRIES

Relevance of strain diversity

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The outcome of infection and disease in TB is highly variable. In addition to host and environmental factors, there is mounting evidence suggesting that strain diversity in *M. tuberculosis* accounts for some of this variability. Here I review and discuss the current evidence for the effect of *M. tuberculosis* variation in TB outcome, and highlight the need for a phylogenetically robust framework for classification of *M. tuberculosis* isolates based on whole genome sequencing data. Such a framework is fundamental for linking *M. tuberculosis* genotype to experimental and clinical phenotypes, and unrevealing the true relevance of *M. tuberculosis* strain diversity for TB control.

Molecular epidemiology of *M. tuberculosis* in Malawi

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Aim: To give an overview of *M. tuberculosis* strain diversity in a rural African population, including changes over a 20 year period and associations between strains and markers of virulence and transmissibility.

Methods: The Karonga Prevention Study in northern Malawi includes detailed data on all TB cases in the district since 1986. Molecular typing (RFLP and some spoligotyping) has been done on isolates from all patients from 1996, and on available smears back to 1986 (spoligotyping). PCR has been used to investigate mixed infection and a whole genome sequencing project is underway. Spoligotype results were used to classify strains into the 4 lineages.

Selected findings: All 4 lineages are present in this population. Lineage 4 (LAM) strains predominate, but have decreased over time (from >90% to 60%), with increases in the other 3 lineages. Lineage 2 (Beijing) was first found in 1991 and increased to 4%. Lineages 1 and 3 both increased from about 4% to 16%. Lineage 1 strains were more common in those with HIV infection. No associations were found between lineage and drug resistance or outcome or transmissibility.

Conclusions: In this population all first episodes of disease due to Beijing strains were fully drug sensitive. Beijing strains accounted for recurrence due to reinfection disease more often than would be expected by chance. Using PCR techniques, mixed infections were rare and no instances were found where Beijing strains were mixed with non-Beijing strains.

Mycobacterium tuberculosis spoligotypes and drug susceptibility pattern of isolates from tuberculosis patients in an HIV endemic area

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Setting: Peri-urban Kampala, Uganda.
Objective: To determine the predominant strain lineages causing TB in a peri-urban population of Kampala, and to study associations between *M. tuberculosis* strain types, anti-tuberculosis drugs and HIV sero-status of the patients.
Design: We consecutively enrolled 344 consenting adult TB patients attending clinics in Rubaga Division. Sample processing and culture were performed at the National TB Reference Laboratory and molecular assays at Makerere Medical School. Species identification was achieved by determining regions of difference (RDs); strain types were uncovered by standard spoligotyping and comparison with the international spoligotype database (SpolDB4), while anti-tuberculosis drug susceptibility assays for isoniazid and rifampicin were performed by the indirect proportion method on Löwenstein-Jensen media. Associations between drug resistance, HIV sero-status and the most predominant strain types were determined using STATA v.11.
Results: Of the 344 isolates, 343 (99.7%) were *M. tuberculosis*, while one was classical *M. bovis*. Furthermore, 241 (70.2%) of the *M. tuberculosis* isolates were of the T2 family as determined by spoligotyping, while CAS1-Kili (3.5%), LAM9 (2.6%), CAS1-Delhi (2.6%) were the other significant spoligotypes. The T2 family was in turn predominated by a spoligotype specific and RD724 deleted strain type now known as Uganda genotype. A total of 92 of the 168 patients who consented to HIV testing were HIV sero-positive. Resistance to isoniazid was found in 8.1% of strains, while all 15 (4.4%) strains resistant to rifampicin were also resistant to isoniazid, hence multidrug resistant. Strain types were neither associated with drug resistance nor HIV sero-status.
Conclusion: *M. tuberculosis* is the most prevalent species of the *M. tuberculosis* complex in Kampala while the Uganda genotype is the predominant strain.

Strain diversity in South Asia and association with drug resistance

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Aim: To evaluate *M. tuberculosis* (MTB) genotypes prevalent in South Asia with a particular focus on Karachi, Pakistan. Association between genotypes and drug resistance was studied.
Methods: 1004 MTB strains from field sites in Karachi collected during 2006–2009 were spoligotyped. Amongst the predominant genotypes 55% were Central Asian strains (including, 37% ST26 CAS1_Delhi), 10% East African-Indian (EAI), 3.0% Harlem and 3% Beijing genogroups.
Results: Overall multi-drug resistance (MDR) rate was 4.3%, 95%CI 3.0–5.5% (untreated 2.4%, treated 14.0%). Isoniazid mono-resistance was 3.5%, 95%CI 2.4–4.6% (untreated 3%, treated 6.3%). MDR was significantly associated with the Harlem genotype (OR 9.2, 95%CI 3.6–23.8). Association between the Harlem genogroup and isoniazid mono-resistance however could not be shown. Similarly, no association was observed between MDR and the prevalent CAS family strains.
Conclusion: Our data suggests association between MDR and Harlem strain types in Karachi. This differs from published nationwide data suggesting association between MDR and Beijing genogroup. Our studies therefore indicate local variation in genogroups contributing to drug resistance within the region.

New forms of totally drug-resistant *M. tuberculosis*

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Setting: Mycobacteriology Research Centre, National Research Institute of Tuberculosis and Lung Diseases, Tehran.
Objective: The complexity of resistance to second-line drugs in totally drug resistant (TDR) or extremely drug resistant tuberculosis (XXDR-TB) raises the possible morphological changes that may occur at the ultra structural level.
Design: Isolates from each group of susceptible, MDR, XDR-TB and XXDR-TB strains were observed under transmission electronic (TEM) and atomic Force microscopy (AFM).
Results: Transmission and atomic force microscopy revealed shape transformation in XXDR-TB cells.
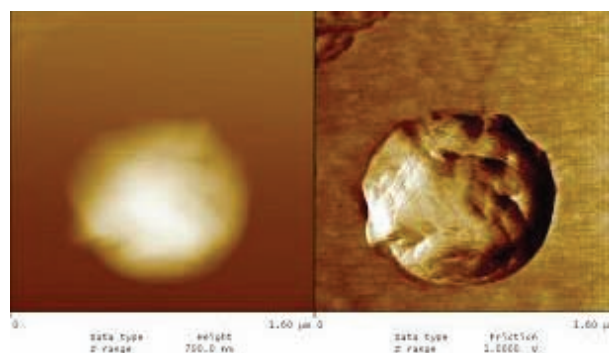
More than 45–50% of XXDR-cells were oval or round shape with average dimension of 0.3–0.9µ and 0.2–0.5µ, respectively. These round cells were different from buds or polar division, being similar to terminal endospores of which they did not present the typical heat resistance.

Conclusion: It is important to evaluate the possibility of diseases transmission through round or oval shape XXDR-TB bacilli. They are smaller in comparison to rod shape bacilli and would transfer in faster rate. Therefore, the XXDR-TB is a dangerous form of TB and it requires the urgent attention from the global scientific community.

Mycobacterium tuberculosis genotypes from India: implications for TB control programmes

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Tuberculosis (TB), caused by *Mycobacterium tuberculosis*, continues to be the leading source of mortality and morbidity across the world with India fast emerging as the TB capital of the world. In order to develop effective intervention strategies it is equally important to focus not only on a system of information and efficient methods for localizing sources of infection, but also highlight tools that enable enhanced understanding of the dynamics of spreading of disease. Accurate identification of the underlying strains in an epidemiological setting is therefore of paramount significance. There is no scientific evidence to explain that some strains of the TB bacilli spread faster and transmit more aggressively than others although strains such as *M. tuberculosis* Beijing/W have been widely reported to cause large scale and fatal outbreaks perhaps linked to their postulated propensity to transmit faster. This presentation provides an overview of the present scenario of molecular epidemiology and dissemination dynamics of *M. tuberculosis* in India and discuss how systematic, genome sequence based methods allow decipherment of the population genetic structure of *M. tuberculosis* which was not achievable with traditional fingerprinting methods. It will also be relevant to discuss the prevalence of ancestral genotypes in India which perhaps represent less disseminating and more controllable lineages that infect a majority of TB patients in this high burden country.

PROGRESS TOWARDS TB ELIMINATION IN THE EU AND BEYOND: SHORTCOMINGS AND POSSIBLE SOLUTIONS IN TB CONTROL

New tools for control: implementation of molecular epidemiological parameters in contact tracing

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Background/aim: To investigate the significance of genotyping of TB isolates as routine tool for contact tracing in a low-incidence setting in 6 German regions (Hamburg, Berlin, Munich, Hanover, Lower Franconia and the Upper Palatinate).

Methods: A prospective, molecular-epidemiological study was performed. Results of conventional contact tracing and additional patient interviews were used for further epidemiological analyses.

Results: In total, 2270 TB patients were analyzed between 2001 and 2009 (90% of all culture-positive patients). Isolates from more than 33% showed identical IS6110 RFLP/MIRU patterns and were classified into 206 clusters ranging from 2 to 58 patients. Whereas in multivariate analyses alcohol abuse was the strongest independent predictor for clustering, homelessness, foreign ethnicity, sex, drug addiction, and HIV positivity were no independent risk factors.

Contact tracing, performed prior to genotyping, predicted a recent transmission in only about one fifth of clustered patients with retrospectively confirmed or presumed epidemiological links. Vice versa, only about one half of patients in whom transmission links were assumed by classical epidemiological data, were cluster members.

Contact tracing was performed in 1995 index patients. In a subgroup analysis, only 586 out of 4633 contacts (1.3%) were classified as 'infected' based on a Mantoux TST between 2001 and 2004. Only 113 contacts of 31066 investigated persons (0.36%) developed active TB during this period indicating a great number of superficial, falsely included contacts.

Conclusions: Conventional contract tracing alone is insufficient for detecting infection chains. Genotyping may reveal faults in TB control procedures and helps improving its low efficacy. In view of the financial means required for the costly RFLP analysis, a more careful selection of truly exposed contacts is necessary.

Addressing vulnerable populations: TB controls among migrants in low incidence countries

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Setting: Low incidence countries, especially the EU area.
Objective: To discuss how adequate tuberculosis (TB) prevention and control can be ensured in migrants.
Design: Literature review plus questionnaire to selected low incidence countries.
Results: Migrants in low incidence countries include immigrants, migrant workers, refugees, asylum seekers, undocumented migrants and victims of trafficking. Their number varies hugely between countries and change rapidly, recently because of the global economic recession, political conflicts and strict asylum policies.

Migrants contribute a large proportion of TB, most coming from areas with higher incidence. The proportion with HIV and MDR-TB may also be higher in migrants coming from countries where the level is high.

Access to health services may be reduced because many migrants do not have social insurance and cannot afford the cost. For some migrants fear of deportation may reduce access and health staff may be reluctant to see them. Treatment may be challenging in migrants who need basic social support and who are on the move.

The Union made a statement on undocumented migrants in December 2009 to ensure easy access to low-threshold facilities without fear of being reported to the police or migration officials, remind health staff to respect confidentiality, that undocumented migrants with TB should not be deported until completion of treatment, and raise awareness among undocumented migrants about TB. A few governments are implementing such recommendations. In many countries local initiatives have been taken, openly or clandestinely, to ensure access and no deportation while on TB treatment, often by non-governmental organizations.
Conclusions: Since migrants are a key group in TB control in low prevalence countries, governments should ensure proper prevention, diagnosis and treatment of TB, targeting especially persons with low income and undocumented migrants.

Country perspective: controlling and monitoring TB in a low incidence setting

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Following significant declines over the last century, the incidence of tuberculosis in the UK has increased steadily over the last two decades. Rates of disease now exceed 14 per 100 000 and over 9000 cases were reported in 2009. Tuberculosis is unevenly distributed in the population with the majority of cases in major cities and over two thirds in non-UK born persons. Other risk groups include homeless persons, drug users, HIV infected persons and individuals with a history of imprisonment.

The national control effort is based on an action plan which defines ten key areas of action ranging from strengthening surveillance to supporting international action to curb the global tuberculosis burden. Specific measures implemented since the action plan include a national strain typing service, a TB Find and Treat Service in London, a web-based enhanced surveillance system, a programme of tuberculosis research, guidelines on the clinical and public health management of tuberculosis including those for interferon gamma release assays, and the establishment of a national TB reference group by the Department of Health.

The future effort to control tuberculosis will inevitably require continued active case finding targeting high risk groups, the application of new technologies to correctly identify latently infected persons who will benefit from treatment and high quality surveillance.

NEW DEVELOPMENTS WITH RIFAMYCINS: RIFAPENTINE, RIFABUTIN, AND HIGH-DOSE RIFAMPIN

Pharmacokinetics, pharmacodynamics and drug interactions of rifamycins

K E Dooley. Center for Tuberculosis Research, Johns Hopkins University School of Medicine, Baltimore, MD, USA

Rifamycins serve as the cornerstone of TB therapy, largely because of their unique sterilizing activity. Understanding their pharmacokinetic (PK) and pharmacodynamic (PD) properties is essential, both for effective clinical use of these anti-TB agents as well as for research endeavors aimed at developing a rifamycin-based TB treatment regimen of shortened duration. Rifampicin, rifabutin, and rifapentine are all licensed for TB treatment, yet currently-recommended doses may be less than ideal for some or all of these agents. In vitro, animal, and clinical PK/PD studies can help us optimize the use of these important drugs. Because rifamycins are promiscuous inducers of metabolizing enzymes, use of these agents with co-administered drugs, however, can be nettlesome; in particular, drug-drug interactions complicate TB and HIV co-treatment. This presentation will review the pharmacokinetics, pharmacodynamics, and drug interactions of rifamycins currently used for TB treatment—rifampicin, rifabutin, and rifapentine—with a specific focus on comparative pharmacokinetics, optimization of rifamycin dosing, and co-administration of rifamycins with ARVs.

Rifabutin: new plans for access

D Ripin. Clinton Health Access Initiative, Boston, MA, USA

This talk with provide an overview on progress achieved to expand access to Rifabutin for the treatment of TB in patients taking protease inhibitor-containing ART for the treatment of HIV/AIDS. Rifabutin was added to the WHO Essential Medicines List in March, 2009, and recently after, Pfizer, the drug's manufacturer announced an agreement with the Clinton Health Access initiative to make Rifabutin more widely available in developing markets by reducing its price and expanding registrations.

Progress with rifapentine: Hong Kong, EBA and rifaquin

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Setting: Optimal cure rates of the standard 6 month regimen are not always achieved under programmatic conditions in part because the treatment duration is still too long. Adherence could also be improved if the continuation phase was administered once, or twice weekly. It is likely this would also reduce toxicity and the cost of treatment. The long half-life of rifapentine (about 13 hours) raised the possibility that it could be given once weekly. Moxifloxacin is a strong candidate for use as companion drug to rifapentine, as it has a similarly long half-life of about 14 hrs. Murine studies with twice weekly rifapentine with moxifloxacin indicate remarkable sterilising activity particularly as the dose size of rifapentine is increased from 10 mg/kg (equivalent to 600 mg dose in patients of 60 kg) to 15 mg/kg and to 20 mg/kg.

Objectives: To assess whether a treatment regimen containing moxifloxacin (400 mg) substituted for isoniazid in the intensive phase, followed by a once weekly dose of 1200 mg of rifapentine and 400 mg of moxifloxacin in a 4 month continuation phase, and a treatment regimen containing moxifloxacin (400 mg) substituted for isoniazid in the intensive phase, followed by twice weekly doses of 900 mg rifapentine and 400 mg of moxifloxacin in a 2 month continuation phase, will have a relapse rate not inferior to a standard control regimen based on rifampicin and isoniazid and will prevent the occurrence of rifamycin mono-resistance in relapsing HIV positive patients.

Design: Open label randomised controlled clinical trial of 1100 adult patients with newly diagnosed pulmonary tuberculosis, in 6 centres in Africa, ran-

domised to receive either the standard regimen or a 6 or 4 month regimen containing rifapentine in the continuation phase.

Outcomes assessed:
1 Combined rate of failure and relapse.
2 Presence of rifamycin monoresistance (RMR) in relapse cultures of HIV infected patients.
Occurrence of grade 3 or 4 adverse events during chemotherapy.

Rifapentine trials: TBTC and Johns Hopkins

S Dorman. Johns Hopkins University, Baltimore, Maryland, USA

Rifamycins are key components in modern TB chemotherapy, and are considered critical for 'sterilization,' that is, prevention of relapse after cessation of TB treatment. Rifapentine is highly active against *M. tuberculosis*, with minimum inhibitory concentrations lower than those for rifampin and a longer half-life than rifampin. Preclinical studies of tuberculosis treatment in the mouse model have shown that rifapentine administered daily during combination intensive phase TB treatment has potent antimycobacterial activity that is associated with the ability to achieve durable cure without relapse after only about 3 months of total treatment.

The aim of this presentation is to describe recently completed, ongoing, and planned clinical trials of rifapentine-containing regimens being conducted by the U.S. Centers for Disease Control and Prevention Tuberculosis Trials Consortium and by investigators at Johns Hopkins University. The rationale for, design, conduct, and expected timelines for each trial will be described.

IS SCIENTIFIC EVIDENCE ENOUGH TO CHANGE POLICY?

Tobacco control in Germany: explaining the long-standing opposition to moving from scientific evidence to policy change

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Background: Germany is noted within Europe for its remarkable reluctance to implement effective tobacco control policies. We reviewed two explanations commonly proposed, namely tobacco industry donations to political parties and the legacy of the Nazis' opposition to smoking, and examined the politics of tobacco control in detail to explore the reasons for Germany's opposition to stricter tobacco control.

Methods: We analysed reports of the German government, websites, newspaper articles, the published literature, in particular the comparative tobacco pol-

icy literature, and previously confidential tobacco industry documents made available though litigations in the United States.

Results: Our findings suggest that aspects of political culture including the Nazi heritage which has resulted in a dearth of public health research and teaching, institutional factors such as the reliance on industry self-regulation facilitated by Germany's system of corporatist policy-making and interest group politics resulting in direct influence on policy-making played a key role. For decades, the tobacco industry has also successfully used framing strategies for tobacco-related issues to uphold the social acceptability of smoking and thereby undermined the acceptability of tobacco control in Germany. Powerful frames were constructed and spread on economic, political, social and health issues. The influence of the tobacco industry on science and scientists in Germany was a key tool in framing tobacco-related health issues. In addition a phenomenon that we called 'autarkic epistemic isolation' explains why so little policy learning from abroad has occurred.

Conclusions: We suggest that the interplay of numerous factors explains Germany's weak stance which has resulted in a longstanding opposition to moving from scientific evidence to policy change in tobacco control.

STEP-WISE IMPLEMENTATION OF NEW DIAGNOSTIC TOOLS IN HIGH-BURDEN COUNTRIES AND STRATEGIES FOR ASSESSING THEIR IMPACT

Beyond accuracy: addressing the clinical impact of new TB diagnostics

S Dorman. Johns Hopkins University, Baltimore, MD, USA

New TB diagnostic tools that plausibly may be integrated into TB programs are emerging from the development and evaluation pipeline. Rigorous assessments of test accuracy are critical, but alone are insufficient to guide programmatic use. This presentation will describe strategies for assessing the clinical impact of new TB diagnostic tools and the importance of pre-analytical and post-analytical processes in the diagnostic algorithm.

New diagnostic algorithms

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In recent years several novel TB diagnostic methods received WHO endorsement to be used also in resource limited settings such as liquid culture-based growth detection and susceptibility testing, molecular line probe assay testing and rapid speciation by later flow assays. However, there is still no single test that can stand alone for the detection of TB. In order to obtain the best performance of these new laboratory tests and to generate complete and rapid information on a particular patient it is very important to link complementary techniques in an adequate laboratory diagnostic algorithm. The first step when developing a new laboratory diagnostic algorithm is to determine the target patient population. Diagnostic algorithms in industrialized countries usually aim to identify any patient with tuberculosis, while limited resources and the higher incidence of HIV associated and drug resistant tuberculosis in non-industrialized countries require to focus on those patients that are at risk of drug-resistant, multidrug or extensively drug resistant tuberculosis (e.g. treatment failure or default, HIV infected, contacts of drug resistant cases). The development of a laboratory diagnostic algorithm requires a second step namely adapting this linked system to the different levels of the existing diagnostic network and determining which tests should be performed at a particular level of the services. This has to be based on a reliable specimen collection, transportation and LIMS system. In such a system the different testing results should direct the next necessary step to be taken (additional specimen collection, specimen forward for further testing, therapy initiation) and which subsequent diagnostic test should follow at what service level to avoid delays and ensure system efficacy. The presentation is aiming to summarize these questions using practical examples from the field.

ADDRESSING TB AND TB-HIV THROUGH INNOVATIONS IN TB VACCINE DEVELOPMENT, POPULATION STUDIES AND CLINICAL TRIALS

New tuberculosis vaccines in clinical development

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Background: The current TB vaccine, Bacille Calmette-Guérin (BCG), is largely ineffective in preventing adult pulmonary TB disease, and is not recommended for use in infants infected with HIV due to increased risk of serious BCG-related complications. New, more effective TB vaccines that are safe in people living with HIV could have a significant impact on the TB epidemic and on TB-HIV coinfection by preventing TB and by reducing the overall number of people with TB disease, thereby reducing the risk of transmission. **Methods:** Efforts are underway to develop new vaccines to prevent TB. The primary focus is on developing a heterologous prime-boost vaccine regimen that would include replacing BCG with a recombinant

BCG (rBCG) as the prime, and boosting with one of several novel vaccine candidates, including viral vectored and fusion protein vaccines. The goals for a new rBCG and booster candidates include increased efficacy and safety in people infected with HIV as compared to the current BCG.

Results: As of early 2010, 12 vaccine candidates had entered clinical trials and 9 are currently undergoing clinical testing. Two booster candidates, Oxford MVA85A/AERAS-485 and AERAS-402/Crucell Ad35, are now in Phase IIb proof-of-concept studies. Two vaccine booster candidates, Oxford MVA85A/AERAS-485 and GSK M72, have demonstrated preliminary safety and immunogenicity in people living with HIV in early-stage clinical trials, and candidate *M. vaccae* has had some success in HIV+ subjects. One rBCG candidate is currently in clinical trials and a second rBCG candidate is expected to enter clinical trials in 2010.

Conclusions: New TB vaccines could have significant implications in lowering the incidence of TB and TB-HIV co-infection, thereby reducing the tremendous burden of morbidity and mortality associated with these two diseases.

Designing new TB vaccines with higher safety and efficacy

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The current tuberculosis (TB) vaccine, BCG has been given to more than 4 billion individuals and its coverage in infants exceeds 80%. It protects against severe forms of TB in infants; but protective effects in adults are doubtful. The safety profile of BCG is impressive. However, risk of disseminated BCGosis is increased in HIV-infected infants, which led the WHO to recommend that BCG is not given to children with proven HIV status. Thus, BCG faces two major issues: (i) failure to protect against the most prevalent form of the disease, namely, pulmonary TB in adults which is also the most important source of dissemination (ii) safety issues in the HIV-infected newborn. Hence, a safer and more efficacious TB vaccine is urgently needed. Novel TB vaccine design focuses on a pre-exposure vaccine which prevents TB disease outbreak. First, replacement of BCG by recombinant (r)BCG vaccines are being pursued. Second, subunit vaccines given as booster on top of BCG prime are being evaluated. In both cases, BCG is in the center of vaccine research and development. We have developed an rBCG which expresses listeriolysin (Hly) from L. monocytogenes and has a deletion in the urease C gene. This vaccine strain shows superior protection and safety over BCG in preclinical models. The vaccine has successfully completed a phase I clinical trial in Germany and is currently in a phase Ib trial in Sub-Saharan Africa. Future research aims at further improving this vaccine. To increase safety, first auxotrophy is being introduced, second the vaccine candidate is rendered non-replicating but metabolically active. To increase efficacy, anti-apoptotic genes are being deleted to improve cross-priming, genes encoding human cytokines are being added, to improve Th1 and Th17 immune responses and finally additional *Mycobacterium tuberculosis* antigens either absent in, or insufficiently expressed by, BCG are being introduced.

Preparation and considerations for TB vaccine trials in areas of high TB incidence and HIV prevalence

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The natural history of tuberculosis and experience with Bacille Calmette Guerin (BCG) suggests that vaccine prevention of tuberculosis could be achieved in humans. Data from animal models indicates some novel subunit, live and virally vectored vaccines have similar efficacy to BCG and can showed enhanced efficacy when included as part of prime boost regimes that include BCG. The frustrating lack of an immunological correlate of vaccine-induced or natural protection is however a barrier to progress. It has therefore been argued that the situation is sufficiently urgent to undertake clinical trials of novel vaccine efficacy in the absence of such correlates, instead adopting clinical disease as an endpoint. This necessarily high risk strategy is expensive and requires trial infrastructures that are not widely available. High incidence environments have the paradoxical advantage of reduced recruitment and follow-up targets in these circumstances. A further high-risk high-gain scenario is to include persons co-infected with HIV-1: the obvious trade-off being the immunosuppression conferred by HIV-1 infection that will likely reduce vaccine efficacy against yet higher incidence. The generalisability is potentially attractive: if a new vaccine exhibits even partial efficacy in immunocompromised persons subject to high infection pressure, it could be inferred that its efficacy in populations at lower risk might be at least as great. This presentation will therefore review theoretical and practical issues in establishing a trials site in an area of very high TB incidence and HIV-1 prevalence.

HEALTH SYSTEM RESPONSE FOR HUMAN RESOURCES: ENSURING TB WORKFORCE IS PRESENT, COMPETENT, SUPERVISED AND SUPPORTED

Supply of health workforce: retaining staff for TB control

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Settings: National TB control Programme, Malawi.
Objective: Implementing Five Year Development Plan for Malawi NTP 2002–2006; and the Malawi NTP, Human Resource Strategy Plan, 2008–2011 to enhance staff retention for TB control.
Design: The Malawi NTP developed and implemented a five year development plan, 2002–2006, and subsequently Human resource strategy plan for TB control, 2008–2011. The areas of implementation included staff development and training, quality and quantity of training, supervision, quality assurance for the NTP, human resource management information systems, incentives, performance systems and operational research. Further, the NTP established a training sub working group, task and responsibility description for all staff, skills improvement of research activities and implemented quality improvement approach for TB control.
Results: Between 2002 and 2010, the NTP capacity increased its staff key positions from 21% to 90% and retained in position 96% of its staff. The attributes for retaining staff for TB control have been due to the enhancement of competence and motivation of staff, staff performance for their clear task and responsibilities, and strengthened operational research for improvement of programme performance.

Challenges to ensuring a competent workforce within a decentralised health system

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The National Tuberculosis Programme (NTP) in Thailand was established in 1966. In the beginning, the programme was implementing as the vertical programme; subsequently, however, it was changed to an integral part of the existing general health services, aiming to provide countrywide services accessible to the population. The vision and direction of the Thai government accordingly imposed the new policy to downsize the workforces and decentralised the system in 2001. This caused a significant effect to the TB service across the nation. The tangible example could be seen that staff retention time Tb became shorter. The financial support was hard to estimate. In 2002, with the enactment of the National Health Security act and the establishment of the National Health

Security office, as a funding agency to the health service, this brought a significant transform of Thailand's health care system. The Department of Disease control, therefore, has to adapt both its structure and function. In the transitional period, it weakened the existing TB service, for example, the reduction of human resource, no earmark budgeting which eventually affected the training activities and weakening of supervision and monitoring.

The NTP of Thailand has fully concerned to improve health system for human resource in order to ensure TB workforce is present. The major strategies are mentioned as listed:
1 advocacy by evidence base to gain a high level commitment
2 using the health inspections mechanism to facilitate the quality of TB service
3 negotiation with the NHSO to provide additional earmark TB budget
4 accelerate engagement of medical school
5 approach to the hospital accreditation to meet the requirement of ISTC
6 currently 'TB TEAM' is being set up
7 regular monitoring and supervision.

With the stream of reforming in health care system of Thailand, the NTP faced a number of challenges but with hard work, it has passed the period of most difficulties.

LESSONS FROM TB PREVALENCE SURVEYS INTO PRACTICE: EXPERIENCES IN ASIA

Progress Report: TB prevalence surveys

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The Prevalence Survey Group was established in WHO Global Task Force on TB Impact Measurement in December 2007, facilitating preparation, implementation and analytical process of the national TB prevalence surveys in more than 20 countries. Since 2007, 5 countries in Asia completed their national surveys (Philippines, Viet Nam, Bangladesh, Myanmar, China) and several countries plan to launch a survey in 2010 (Cambodia, Ethiopia, Laos, Nigeria, Pakistan, Tanzania).

Surveys can tell us much more than just the prevalence of disease in a country. Past surveys have identified limitations of routine case detection by showing how few are captured by screening of chronic cough and smear microscopy alone. Study subject interviews can also identify characteristics of missing cases—where they are concentrated in a country, how their access to care affects case detection, where they seek care and how they utilize various services. Surveys

can also reveal the role of the private sector in TB care. These findings help identify areas of needed work in national TB programmes, such as improved collaboration with the private sector, and they also help to define areas of operational research that could be of value to the programme. This rich information can then be used to improve NTP services more broadly. In the symposium, we also would like to launch the 2nd edition of the survey handbook to address many of the technical and managerial challenges and to introduce lessons from countries.

Re-estimation of TB burden and its implication to the program in Viet Nam

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Background: WHO estimated that Viet Nam has since 1997 reached the global targets for tuberculosis (TB) control. However, annual notification rates of NSPTB cases have increased until 2004 and have since stabilized. This estimation was based on Styblo's rule using ARTI, therefore the figures might not reflect the true burden of TB in the current conditions. The prevalence of TB as found in a recent nationwide prevalence survey was 1.6 times higher than previously estimated. This finding clearly suggests that we need to re-estimate TB burden and new approaches for TB control.
Objective: Re-estimate TB burden and identify potential solutions to increase case detection of tuberculosis.
Method: The case detection rate (CDR) was re-estimated using 2 methods: (1) calculation through the patient diagnostic rate (PDR) with hypothesis of disease duration as 2 year in average; (2) expert opinion based on 'onion model'. The later method was also used for identification where the missing cases are and how to get them detected.
Results: The prevalence of NSPTB in Viet Nam was 155 (95%CI 119–190) in adults of 15 years and older. In the same population, the notification rate of NSPTB was 93/100 000. We estimated the PDR to be 0.62 (95%CI 0.49–0.78) and the CDR as 0.56 (95%CI 0.41–0.68). Using onion model to guess the size of missing cases, we estimated CDR as 0.52 (95%CI 0.36–0.63). Increase case detection is a key issue of TB control in Viet Nam. The solutions were identified as PPM, PAL, intensified case finding in high risk groups (close contacts, HIV infected, previously-treated cases, IDUs, diabetes) and strengthen ACSM.
Conclusion: National Prevalence survey of TB played very important roles in measuring TB burden and directing TB control program effectively.

Introduction of active case detection in Cambodia

S Peou. National Center for Tuberculosis and Leprosy Control, Phnom Penh, Cambodia

Introduction: To increase the case detection rate that could not reach a target of year plan, the National Center for Tuberculosis has conducted an active case finding nationwide where the people could not access to TB facilities. The active case detection in Cambodia has been conducted 5 times since 2005.
Method: Cases suspected by symptom were identified by village health supporting group (VHSG) and brought for chest X-ray at health centers. The case suspected (4344 patients) from 585 villages were undergoing chest X-ray by the Mobile TB Team of National Center for Tuberculosis. Patient with abnormality of chest X-ray suggestive for TB was requested for three cups of sputum collection (one cup on the spot and two cups at the next morning). The smearing and microscopy examination were done at health center. The diagnosis was released within 2 days to the patient. TB registration and treatments have been done at health center.
Results: The chest X-ray reading was made by the team leader as a physician or radiologist. In 2009, the result of film reading as fellow: TB active (407 cases), TB healed (249 cases), TB suspect (191 cases), other lung and heart diseases (325 cases) and normal chest X-ray were 3178 cases. There were 683 cases requested for sputum collection. Among them, 115 cases were confirmed as smear positive. As the result of active case detection, we found an active pulmonary TB smear positive 115 cases, an active pulmonary TB smear negative 404 cases. The total anti-tuberculosis treatment for pulmonary TB was 519 cases.
Conclusion: With a good collaboration of local staffs especially with the village health supporting groups, the active case detection in 2009 achieved more pulmonary TB cases in particularly pulmonary TB smear negative and could help patients with poor access to the X-ray facilities.

INNOVATIVE SOLUTIONS TO INCREASE EQUITABLE ACCESS AND QUALITY OF TB-HIV CARE IN REMOTE AND ISOLATED AREAS

Pilot innovation to national strategy: sputum collection points to universal access strategy: Malawi

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Setting: Mtsiliza Township. A poor urban city of Lilongwe, Malawi.
Objective: To increase the number of TB patients at community level.

Design: REACH Trust, a local NGO working with the Malawi NTP implemented an innovative approach to increase identification of TB of a local community by working with local leaders, village health volunteers, and ex-TB patients to specifically target poor people. Community sputum collection points (CSCPs) were established to reduce costly visits to health care centers. Community volunteers (CVs) identified people with TB symptoms, collected sputum for diagnosis.

Results: The CSPCs increased to access services at the local community (care seeking for symptoms, diagnosis, and treatment adherence). Achievements were attributed to bringing TB services closer to homes; provision of information, education, and communication about TB. The introduction of community based initiatives helped urban township level health workers to get more involved in TB control Programme addressing health systems barriers by increasing capacity of local health service. The success of the Mtsiliza CSPC pilot was adopted into National Policy and scaled up country wide for implementation.

Controlled scale-up of national policy in Malawi

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Setting: Mulanje and Phalombe Districts, Southern Malawi.

Objective: To present an example of the practical implementation of a new national policy on Universal Access to TB Diagnosis.

Design: The program implemented a community-based strategy using community sputum collection points (CSCP) to increase access to TB testing and diagnostics. Project HOPE collaborated with District Health staff to identify villages and collection sites, train community volunteers, coordinate with nearby health facilities, and supervise and monitor progress of CSCPs.

Results: This initiative contributed to increased case detection and contact tracing by bringing TB education and testing into the communities, in conjunction with other community interventions. Volunteers also indicated increased status within their surrounding communities and have continued to provide education on TB to increase awareness and earlier care seeking. Challenges include timely transportation of sputum and support for volunteers.

Conclusions: Involvement of communities in increasing access to information and detection of TB helps get people into treatment faster and builds a supportive environment for adhering to treatment. It is important to monitor and evaluate the positive impact of CSCPs, as well as to consider potential barriers, to continue to improve access for TB detection and to support the community volunteers in the important role they play in the fight against TB.

Controlled scale-up of national policy in Malawi

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Setting: In Zomba and Mangochi Districts, with a low rate of TB case detection and a high rate of HIV infection. Passive TB case finding is still a norm and does not work for the poor who face innumerable barriers to access care. Community sputum collection points (CSCP) were identified by the National TB Program (NTP) as a potential strategy to address the challenge.

Objective: To present a practical strategy to accelerate 'Universal Access to TB Diagnosis' in resource poor settings.

Design: An integrated TB-HIV community project is implemented in partnership with four community based organizations (CBOs). This approach was chosen because it builds on existing HIV/AIDS care and support services provided by CBOs and offers opportunities for sustainability. CSCP were established in collaboration with NTP and traditional leaders. CSCPs are structures conveniently located in communities so that TB suspects do not travel long distances to submit sputum for testing and timely access results and treatment. FHI Technical Officers and District TB Officers conduct monthly and quarterly supervision.

Results: Over a period of 3 years, 113 CSPC were established in remote areas and 2759 TB suspects submitted sputum. Of these, 255 (9.5%) were smear positive. The proportion represented 14.5% ($n = 1760$) of the total district smear positive cases.

Conclusions: The limited accessibility of TB microscopy sites is a serious hindrance to TB care for poor people.

Analysis of efficacy and effectiveness of community sputum collection points, a good solution?

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Setting: Phalombe, Mulanje, Zomba and Mangochi districts in Southern Malawi.

Objectives: Determine the efficacy and effectiveness of community sputum collection points in Southern Malawi for nationwide scale-up.

Design: Involving communities in efforts to improve TB control is essential for improving case detection and increasing demand for equitable access to TB services, especially in more remote settings. Reach Trust implemented a pilot of community sputum collection points (CSCP) in the Mtsiliza community on the outskirts of Lilongwe, Malawi. The pilot proved to be successful by increasing the direct access of the

community to TB diagnostic services. Based on the lessons learned, a national policy was developed to implement CSCPs across all of Malawi. To date only a few districts have implemented CSCPs, four of which are supported by Project Hope and TB CAP.

Description: This presentation specifically focuses on the experiences of Project Hope and TB CAP to implement CSCPs. A comparative analysis will be used to discuss the two approaches used, their results and recommendations for further scale-up.

Results and conclusions: The following questions will be addressed:

1 Are CSCPs an effective approach to increasing TB case finding?
2 Are CSCPs valuable in creating greater efficacy among the community?
3 Using qualitative and quantitative data, what are the added benefits of each approach?
4 Recommendations on how to move from district pilot sites to National scale-up.

Short message service for health education, adherence and mobile image transfer: Uganda results

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Setting: Rural health care clinics, such as those found in Sub-Saharan Africa, are typically under-staffed and lack training and support. Microscopes are the main instruments used for diagnosis of infectious diseases, and while they are available at most levels of health clinics, the lack of education, confidence (other) resources and experience amongst the staff are the main grounds for misdiagnosis of illnesses which is a cause of inappropriate treatment and thus poor patient care. These challenges will be addressed by combining microscopy with mobile networks (MobiScopy). This system will create a knowledge sharing forum specifically designed for rural health care workers to improve microscopy based diagnostics.

Objectives/expected benefits: Reduction of costs for quality assurance (QA) and increased compliance. Strengthened education of rural health care workers and improved diagnosis of illnesses and proper treatment. Creation of local business opportunities by franchising MobiScopy to other developing countries.

Design: Selection of regional/reference hospital and five remote satellite health centre laboratories. Improvement of current quality control procedures can be determined by evaluating the existing and novel systems concurrently over a period of time.

Conclusions: Under-educated and under-experienced health care workers will be empowered to meet quality assurance standards and accurately and confidently diagnose parasitical and bacterial infections and receive health education where necessary.

Increasing connectivity of isolated health workers in poor countries using locally available technology

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Setting: We previously showed that images from a microscope can be easily taken and sent for remote reference with m-phones, without any adaptor.

Aim: Testing the viability of our Mobile Diagnosis approach in poor resources settings, and validating health-care applications beyond the laboratory and in extension services.

Methods: We tested Mobile Diagnosis with local health workers in rural areas of two developing countries. Multimedia Messaging Services (MMS) availability and local use was verified. Structured interviews helped to define local diagnostic capacities, workload, extension services, use of clinical and laboratory equipment, availability and use of m-phones, and others. In Uganda (Lacor) 20 trained lab-technicians and 25 trainees were involved. In Bangladesh (rural districts of Bhuapur and Comilla) 16 lab-technicians and 6 medical doctors (GPs) participated, as well as the Grameen Kalyan's reference center in Dhaka where images were received and diagnosis confirmed. Mobile Diagnosis was tested as didactic tool.

Results: Where there was a laboratory there was a technician and a microscope, often inadequately used for lack of training. Use of integrated camera m-phones was widely spread. MMS commonly accessible in Bangladesh, less so in rural Uganda, however not used in both, costs and setting procedure being possible obstacles. Clinical and microscopy use of m-phones was previously unknown, but easily learnt. Microscopy images on the m-phone screen proved to be an excellent educational tool. Mobile Diagnosis was readily extended to dermatological, radiological and ultrasound diagnostics. Different cultural attitudes toward the use of available equipment were noted between Bengali and African health workers.

O-stained sputum samples from tuberculosis suspects in San Francisco and Uganda. Preliminary testing demonstrates that CellScope is capable of high quality digital imaging of sputum smears—sub-micron resolution enables visualization of the characteristic beaded appearance of tuberculous bacilli. CellScope is a powerful new tool that brings fluorescence imaging into the digital era. This technology has the potential to dramatically expand access to TB diagnostic services, facilitate training and quality assurance programs, and enhance tuberculosis surveillance activities.

TOBACCO AND LUNG HEALTH: EVIDENCE FOR INCREASED RISK OF TB, PNEUMONIA, AND ASTHMA IN CHILDREN AND ADULTS

Smoking and the risk of community-acquired pneumonia, bronchiolitis and asthma

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Smoking is a major risk factor for a number of medical conditions, which is not surprising given its significant effects on the body, including interactions with both innate and adaptive immunity. In asthmatics, studies have clearly shown that 1) smoking is more prevalent among individuals with asthma than among those without the disease, 2) smoking itself is a risk factor for the development of asthma, and 3) smoking is associated with a decrease in overall asthma control, a decreased response to agents such as inhaled and oral corticosteroids, and an increased risk of asthmatic attacks, exacerbations and mortality. Bronchiolar disorders are a myriad of conditions that variously effect adults and children and a number of these are associated with smoking. For example, respiratory bronchiolitis is one of the most common causes of the primary bronchiolar disorders and most cases are associated with cigarette smoking in adults. In children there is very good evidence that environmental cigarette smoke exposure is a risk factor for bronchiolitis, including that caused by Respiratory Syncytial virus, which also worsens the severity and prognosis. A number of studies over a considerable period of time have documented that smoking predisposes patients to community-acquired pneumonia (CAP), in general, and pneumococcal infections in particular. This increased risk is demonstrated in HIV-infected persons as well, and persists even after the initiation of anti-retroviral therapy. A decrease in smoking exposure has been shown to be associated with a decrease in the prevalence of a number of these conditions, as well as a decrease in their severity if present in patients who previously smoked.

Conclusions: Mobile Diagnosis may contribute to increase quality of diagnostics and care, but challenges rest in education, initiative, organisation and understanding of local context, rather than in costly new technology.

Mobile phone based clinical microscopy for global health applications

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Sputum smear microscopy is the clinical standard for tuberculosis (TB) diagnosis in many developing countries. However, microscopy services are currently confined to centralized health centers and require trained laboratory personnel. Mobile fluorescence imaging coupled with wireless transmission presents an opportunity to overcome these barriers to rapid and inexpensive point-of-care TB diagnosis. We have developed a mobile digital fluorescence imaging system called CellScope that enables point-of-care TB microscopy. Originally based on a standard camera phone platform, we have recently built a stand-alone device coupled with an inexpensive netbook computer that has significantly improved optical performance. CellScope has several potential advantages over traditional microscopy: (1) portability allows microscopy services to be provided at a patient's doorstep; (2) battery-powered LED illumination enables both brightfield and fluorescence imaging in daylight; (3) digital image processing enhances identification of bacilli; (4) automated reading algorithms reduce the need for trained microscopists; and (5) wireless connectivity allows images to be transmitted over cellular networks for interpretation by trained personnel or for external quality assurance. We are currently refining the second-generation CellScope using Auramine

Smoking and tuberculosis in China

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Male smoking prevalence is very high in many parts of China. Despite successful implementation of DOTS, the annual tuberculosis (TB) notification rate is around 80/100 000 in Hong Kong, while the prevalence of pulmonary TB was 367/100 000 in a survey undertaken in 2000 in Mainland China. In a prospective community cohort of 42 655 elderly subjects in Hong Kong, the annual TB notification rates were 735, 427, and 174/100 000 among current smokers, ex-smokers and never-smokers respectively. A statistically significant and independent dose-response relationship was also observed among current smokers. The excess risk applied to pulmonary but not extrapulmonary TB. Smoking cessation almost halved the risk. Smoking accounted for 32.8%, 8.6% and 18.7% of the TB risk among males, females and the whole cohort respectively. About 45% of the gender difference was attributable to smoking. In another prospective cohort involving 15 486 elderly female never-smokers living with their surviving husband, passive exposure to secondhand tobacco smoke was independently associated with the development of both active TB (HR, 1.49; 95%CI 1.01–2.19) and culture-confirmed TB (HR, 1.70; 95%CI 1.04–2.80). Passive smoking accounted for 13.7% of active TB and for 18.5% of culture-positive TB. Smoking also affects the clinical presentation of tuberculosis. More aggressive pulmonary involvement, with more cough, dyspnoea, upper zone involvement, cavity, miliary lung involvement and positive sputum culture, has also been found among ever-smoking TB patients in comparison with never-smokers.

In a time-based, multiple risk factor modelling study, complete cessation of smoking and solid-fuel use in China would reduce the projected annual tuberculosis incidence in 2033 by 14–52% even in presence of 80% DOTS coverage. Measures on tobacco control should therefore be considered alongside DOTS in the fight against TB.

ABSTRACT PRESENTATIONS SATURDAY 13 NOVEMBER 2010

FEATURED ABSTRACT PRESENTATIONS

RESEARCH IN TUBERCULOSIS DIAGNOSIS

FA-101060-13 ESAT6-induced IFN-γ, CXCL9, CXCL10 and CCL2 differentiate severity of tuberculosis

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Background: T cell and macrophage activation is essential for immunity against *M. tuberculosis*. ESAT6-induced IFN-γ responses are predictive of tuberculosis (TB) but have limited utility in endemic settings therefore additional biomarkers are required for increased efficacy of ESAT6-based TB diagnosis.
Methods: ESAT6 antigen stimulated whole blood cells from TB patients ($n = 79$) with pulmonary (PTB, $n = 36$), localized extrapulmonary (L-ETB, $n = 31$) or disseminated ETB (D-ETB, $n = 12$) disease were assessed for secretion of IFN-γ, CXCL9, CXCL10 and CCL2 responses. 33 healthy endemic controls were also studied. Cut offs were at $2 \times$ SDEV of unstimulated levels in each case.
Results: ESAT6-induced IFN-γ responses revealed 31% responders amongst PTB; 35% amongst L-ETB, none in D-ETB and 15% in ECs. ESAT6-induced IFN-γ was higher in L-ETB as compared with PTB ($P = 0.029$). ESAT6-induced CCL2 was greater in PTB as compared with D-ETB ($P = 0.04$). ESAT6-induced IFN-γ, CXCL9 and CXCL10 responses were all absent in patients with D-ETB. Within PTB disease severity, IFN-γ was greater in minimal as compared with moderate ($P = 0.021$) and far advanced ($P = 0.014$) disease, using Mann-Whitney U analysis. However, ESAT6-induced CXCL9 increased in advanced PTB as compared with moderate disease ($P = 0.04$). Overall, there was a positive correlation between IFN-γ and CXCL9 ($r^2 = 0.454$, $P < 0.001$); CXCL10 ($r^2 = 0.515$, $P < 0.001$) and CCL2 ($r^2 = 0.245$, $P = 0.03$) responses in TB patients.
Conclusion: ESAT6-induced IFN-γ responses have limited utility to predict TB in an endemic setting. However, ESAT6-induced IFN-γ, CXCL9, CXCL10 and CCL2 responses differ according to the severity of TB in patients and are reflective of disease progression in the host.

FA-101138-13 Finding new mutations of rifampin and isoniazid resistant-associated genes in *M. tuberculosis*

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Background: In Taiwan, approximately 2.6% and 8.9% of multidrug resistant (MDR) *Mycobacterium tuberculosis* did not harbor mutations in the hot-spot region of the *rpo*B gene for rifampin (RMP) resistance, and in the *kat*G, *inh*A, *inh*Ar, and *oxy*R-*ahp*C genes for isoniazid (INH) resistance. The aim of this study is to identify new mutation sites of resistant-associated genes to improve the detection of MDR *M. tuberculosis*.
Methods: Drug susceptibility test (DST) of *M. tuberculosis* was performed using agar proportion method and gene sequencing by an ABI 3730 automated sequencer (Applied Biosystems, USA) using standardized conditions. Ten RMP resistant *M. tuberculosis* isolates harboring no mutations in the *rpo*B hot-spot region and 31 RMP susceptible isolates were analyzed in *rpo*B gene codon 176. Besides, 60 INH resistant *M. tuberculosis* isolates harboring no mutation in the *kat*G, *inh*A, *inh*Ar, and *oxy*R-*ahp*C genes and 19 INH susceptible isolates were investigated in the *fur*A, *ndh*, kasA, mabA, efpA, Rv0340, iniB, iniA, and iniC genes.
Results: Of the ten *M. tuberculosis* RMP resistant isolates, seven (70.0%) had mutation in *rpo*B codon 176 (Val to Phe). This mutation was not identified in thirty-one RMP susceptible isolates. We identified 14 mutation sites in INH resistant (30.0%, 18/60) but not in susceptible isolates, including three known mutation sites (12-bp deletion in iniB codon 222, mabA −15 C to T, and −17 G to T) and 11 novel sites.
Conclusions: With the findings of novel alleles of RMP and INH resistant genes, we can increase 4.5% of MDR *M. tuberculosis* detection rate.

FA-101098-13 Detection of TB using the Cepheid Xpert MTB/RIF® Assay: a clinical validation study from Tanzania

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Background: Tuberculosis (TB) control is hampered by inadequate diagnosis, especially in resource-poor countries. New, rapid and simple-to-use diagnostic

tools are desperately needed. Here we evaluate the Xpert MTB/RIF® test (Cepheid, USA), a cartridge-based real-time PCR assay that automates sample processing, amplification, detection of *M. tuberculosis* and resistance to rifampicin.

Methods: 292 consecutively enrolled patients were classified as TB positive or negative following results of sputum smear, solid or liquid culture on three different sputum samples and resolution of symptoms on follow-up one and two months after initial assessment. The Xpert MTB/RIF® test (Xpert) was performed on two frozen, untreated sputum samples per patient.

Results: Of 69 culture-positive (LJ and/or MGIT) TB cases, 88.4% were detected by Xpert (95%CI = 78–95%). There was a marked difference in sensitivity between smear-positive and only culture-positive patients, with sensitivities of 100% and 62% (95%CI = 38–82%) respectively. In accordance with susceptibility testing in liquid culture, no rifampicin resistance was detected by Xpert. Among all TB negative patients, Xpert detected one positive result (99% specificity). One of the samples from 45 patients that were culture-positive for non-tuberculous mycobacteria (NTM) was tested positive by Xpert. Additional analysis is underway to elucidate on these results.

Conclusion: This study evaluates the Xpert in a cohort of consecutively enrolled TB-suspected patients and simulates a typical clinical setting. We demonstrated that the utilization of the Xpert can increase the number of microbiologically identified patients significantly, compared to microscopy, the standard diagnostic procedure in most developing countries. With its easy-to-use technology, Xpert has the potential to play an important role in combating the TB epidemic. Further studies are needed to confirm its performance on fresh sputum samples and on other clinical material.

FA-100915-13   A comparison of the QuantiFERON® Gold In-Tube assay with the tuberculin skin test in infants

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Aim: To compare the QuantiFERON®-TB Gold In-Tube (QFT) assay with the tuberculin skin test (TST) to detect TB infection and disease in infants 1–24 months of age.

Setting: A rural vaccine field site in South India.

Methods: Part of a prospective cohort study aimed at assessing the cumulative incidence of TB disease in infants. Infants received BCG vaccination within 3 days of birth. During follow-up, 682 infants underwent examination with TST and QFT, chest X-ray, smear and culture analysis of 2 induced sputum samples and gastric aspirates.

Results: 166 infants had symptoms suggestive of TB, 524 had failure to thrive and 60 had a recent history of TB contact; 68 had a combination. 6.7% were TST positive (+) using a cut off ⩾10 mm, 42.7% were TST+ using a cut off ⩾5 mm, 4.5% were QFT+, while 3.8% were QFT indeterminate. 24% of TST+ infants were also QFT+ while 36% of QFT positive infants were TST+. The overall agreement at TST cut off ⩾10 mm between the tests was fair (92%, kappa 0.245, 95%CI 0.053–0.436). The agreement between tests at the TST ⩾ 5 mm cut off was poor (60%, kappa 0.07, 95%CI −0.019–0.151). A history of contact with TB was associated with increased odds of being TST+ (OR 3.76, 95%CI 1.68–8.27, $P < 0.001$) and QFT positive (OR 4.01, CI 1.56–10.01, $P < 0.001$). Of 11 infants diagnosed as having definite/probable TB, 1 had a concomitant + TST and QFT, 5 had a TST ⩾ 5 mm but ⩽10 mm and 5 infants had a TST < 5 mm. The QFT test was indeterminate in 2 and negative in 8.

Conclusions: Concordance of TST/QFT was modest in BCG vaccinated South Indian infants. Positive TST and QFT were significantly associated with a history of TB contact. Although, few infants had TB, both tests appear to have suboptimal sensitivity in very young children.

FA-101237-13   Standard mycobacterial decontamination protocols may be inappropriate for samples from paediatric patients

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Background: Liquid based culture is the gold standard for diagnosing TB. Non sterile samples require decontamination, usually with NaOH. Too harsh a decontamination kills mycobacteria, while under-decontamination results in high contamination rates. NaOH concentrations used for processing samples from adults may be inappropriate for paucibacillary samples such as those from paediatric patients. This study aimed to assess the difference in contamination rates and mycobacterial yield of paediatric specimens using two different NaOH concentrations.

Methods: The microbiology laboratory at Groote

Schuur Hospital, Cape Town performs mycobacterial culture using the MGIT system (Becton Dickinson). Non-sterile samples are routinely decontaminated with NaOH N-acetyl-cysteine (final concentration NaOH 1.5%). Contamination rates are between 6 and 8%. For a 6 week period, all samples from Red Cross Children's Hospital (RCCH) were decontaminated with 1% NaOH. Contamination rates and mycobacterial yield were compared to those of adult samples, as well as to those of RCCH samples for the previous 18 weeks (1.5% NaOH).

Results: Results are shown in the Table. Paediatric samples decontaminated with 1% NaOH had similar contamination rates, but a higher culture positivity rate (9.7% vs. 6.0%, $P < 0.01$). One of the main drivers of this difference was the difference in culture positivity among NPA samples (15.2% vs. 3.2%, $P = 0.01$). Contamination and culture positivity rates for adult samples did not differ significantly during the 6 week test period from the preceding 18 weeks.

Table Contamination and culture positivity rates among paediatric samples decontaminated with 1.5% and 1% NaOH

	No of samples		Contamination rate			Culture positivity rate		
	1.5%	1%	1.5%	1%	P value	1.5%	1%	P value
All samples	1825	536	8.1%	8.2%	0.9	6.0%	9.7%	0.003
Resp tract	678	200	6.3%	6.5%	0.9	7.8%	10.0%	0.3
Gastric aspirates	815	207	7.6%	9.7%	0.3	4.0%	4.8%	0.6
NPA	124	46	4.8%	8.7%	0.5	3.2%	15.2%	0.01

Conclusion: The results suggest that specimen processing practices may need to be adjusted in certain paediatric samples with less stringent decontamination processes being more appropriate. Whether such considerations apply to HIV infected patients needs further research, as does the possibility of lowering NaOH concentrations below 1% in paediatric samples.

FA-100230-13 Determining ofloxacin critical concentration in Löwenstein-Jensen medium by absolute concentration method

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A critical concentration of ofloxacin was determined using a panel of 49 genetically heterogenous *M. tuberculosis* cultures analyzed before for mutations in the target genes gyrA and gyrB. The genetic heterogeneity of the cultures was confirmed by RFLP-IS*6110* and MIRU-VNTR typing. The panel comprised 'probably drug-susceptible' and 'probably drug-resistant' *M. tuberculosis* cultures. 'Probably drug-susceptible' cultures were isolated from sputum specimens of ofloxacin untreated patients carrying no mutations

in the *M. tuberculosis* target genes. 'Probably drug-resistant' cultures were from sputum of individuals, who had been treated with ofloxacin for over one month and carried mutations in the *M. tuberculosis* target genes. The critical concentration was determined at the curve change on the basis of minimal inhibiting concentrations (MIC). The latter were established both for 'probably drug-susceptible' and 'probably drug-resistant' *M. tuberculosis* cultures by making serial two-fold dilutions of the antibiotic in Löwenstein-Jensen medium. Based on ofloxacin MICs determined for *M. tuberculosis* clinical strains by method of absolute concentrations, the drug concentration of 3 μg/ml was identified as a critical one. The drug critical concentration was a concentration that either inhibited the growth of more than 95% of 'probably drug-susceptible' or provided the growth of more than 95% of 'probably drug-resistant' *M. tuberculosis* strains.

FA-101140-13 Evaluation of GenoType MTBDRsl assay and gene sequencing in second-line drug susceptibility testing

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Aim: To assess two nucleic acid sequence-based methods for rapid detect second line anti-tuberculosis drug resistance of multidrug resistant (MDR) *Mycobacterium tuberculosis*.

Methods: A total of 68 clinical MDR *M. tuberculosis* isolates were evaluated. The GenoType MTBDRsl assay (HAIN Lifescience, Nehren, Germany) can detect resistance to fluoroquinolone, injectable drugs (kanamycin, capreomycin or amikacin), and ethambutol. MDR isolates were comparatively analyzed using gene sequencing (gyrA, rrs and embB) and the conventional agar-based drug susceptibility testing (DST). The conventional DST was done in parallel by two separate laboratories.

Results: By the conventional DST method, 79.4% (54/68) of MDR *M. tuberculosis* were ethambutol resistance, 88.2% (60/68) were fluoroquinolone resistance, and 35.3% (24/68) were aminoglycosides resistance, including 35.3% (24/68) to kanamycin, 17.6% (12/68) to capreomycin, 23.5% (16/68) to amikacin. However, the MTBDRsl assay only detected 48.1% (26/54) ethambutol resistance, 70% (42/60) fluoroquinolone resistance, and 54.2% (13/24) aminoglycosides resistance, including 54.2% (13/24) kanamycin resistance, 66.7% (8/12) capreomycin resistance and 75% (12/16) amikacin resistance. Gene sequencing could identify 51.9% (28/54) ethambutol resistance, 70% (42/60) fluoroquinolone resistance and 54.2% (13/24) aminoglycosides resistance. The predominant drug-resistance mutation for fluoroquinolone, aminoglycosides and ethambutol were gyrA D94G

(30%, 18/60), rrs A1401G (54.2%, 13/24) and embB M306V (31.5%, 17/54), respectively.

Conclusion: The two nucleic acid sequence-based methods were not applicable in our setting. To improve the sensitivity of the methods, we suggest including more drug-resistance associated genes.

PROGRESS IN HIV AND TB PROGRAMME LINKAGES

FA-100987-13   Tuberculosis and HIV infection in prison institutions of St. Petersburg, Russian Federation

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Background: Morbidity with tuberculosis (TB), prevalence of multidrug-resistant (MDR) TB and the burden of TB and HIV co-infection among prisoners worldwide is significantly higher than in civil population.
Setting: Central regional prison hospital in St. Petersburg, Russia.
Study design: We retrospectively reviewed case records of 196 patients with new culture-positive TB cases, who were admitted for in-patient treatment between January 1, 2005 and September 30, 2009. As much as 132 (67.3%) of the patients were HIV-seropositive (TB-HIV). None of them obtained anti-retroviral therapy prior to detection of TB. Eighty-eight patients had MDR-TB. We reviewed annual distribution of the TB-HIV co-infection cases, see Figure.
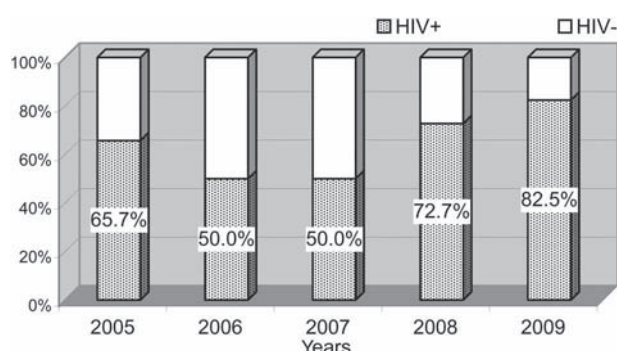
Results: The annual value of TB-HIV patients varied during the last five years. Still the burden of TB-HIV was very high, at least each second TB patient admitted annually had co-infection, with alarming increase of TB-HIV to 82.5% by the last quarter of 2009 ($P = 0.00525$).
Conclusions: During the study period, value of TB

and HIV co-infection among new in-patient TB cases in the penal institutions of St. Petersburg region was very high. However, tendency to further increase during 2008 and 2009 was observed. Introduction of anti-retroviral therapy among HIV-infected prison population is required.

FA-100374-13   Nationwide scale-up of HIV-TB collaborative activities in India

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Background: In India, an estimated 95240 tuberculosis (TB) patients per year also suffer from HIV infection. To reduce the burden of HIV-associated TB, in 2007 the Revised National TB Programme (RNTCP) and the National AIDS Control Programme (NACO) developed a national TB-HIV policy framework.
Response: Since 2007, 9 high HIV-burden states (population of 325 million) have used co-ordination mechanisms and joint trainings to implement intensified TB case finding (ICF), routine referral of all TB patients for voluntary HIV counseling and testing, and provision of free cotrimoxazole preventive therapy (CPT) and antiretroviral treatment (ART) for HIV-infected TB patients. We reviewed routine programme surveillance data to evaluate the impact of policy implementation efforts.
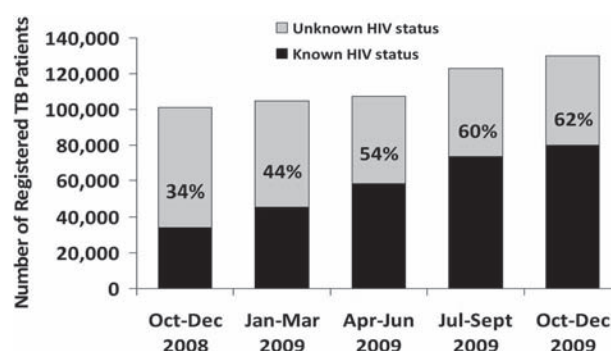
Figure Increase in proportion of TB patients with HIV status known before or during TB treatment, South and North-East India, 2009 (population 325 million, states of Andhra Pradesh, Delhi, Gujarat, Karnataka, Maharashtra, Manipur, Mizoram, Nagaland, and Tamil Nadu).

Results: From 2007–2009, HIV services markedly expanded; integrated HIV counseling and testing centres (ICTCs) grew in number from 4027 to 5135, and ART centres from 107 to 230. Over 3 years, 625 108 ICTC clients were identified as TB suspects through ICF (5.1% of clients counselled), amongst whom 83585 TB cases were detected, representing 6.7% of

all TB cases registered in the respective 9 states. In the past year, the proportion of TB patients with known HIV status increased from 34% to 62% (Figure). Of 107 497 registered TB patients during April–June 2009, 9537 (9%) were HIV-infected, amongst whom 7215 (76%) and 3726 (39%) received CPT and ART respectively during TB treatment.

Discussion: Through intensive collaboration and training, TB-HIV activities have been successfully integrated into the core activities of both programmes. Decentralized HIV testing services in general health facilities are essential to achieve high levels of uptake of HIV testing of TB patients. The increasing coverage of HIV testing among TB patients is encouraging, but provision of ART requires strengthening. RNTCP and NACO are expanding these TB-HIV services nationwide, and expect to achieve full national coverage by 2012.

FA-100454-13 Lessons learnt in implementing HIV prevention services In TB and HIV care settings in Kenya

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Background: Prevention with Positives (PwP) are interventions designed to support HIV-infected persons reduce risk of transmitting HIV. Routine HIV testing among TB patients in Kenya expanded from 20% in 2005 to >80% in 2007; 50% are co-infected. Prevention of new HIV transmissions is critical to long term TB and HIV control. Kenya is currently expanding PwP services in TB-HIV care settings against a background of constrained infrastructure, manpower, and competing service delivery priorities.

Intervention: Kenya TB-HIV programs held multisectoral meetings to set PwP priorities and design an implementation road map in April 2008. Job aids, standard operating procedures, and monitoring tools were developed to support staff training for demonstration projects in selected TB-HIV clinics. PwP messaging included disclosure, partner testing, ART adherence, condom use, referrals, and risk reduction counseling.

Results and lessons learnt: PwP interventions, e.g, disclosure and partner testing, were initiated in TB clinics nationally. In 2008, 6712 (16%) of the 41 950 reported HIV-TB-infected patients invited partners for HIV testing or reported partner serostatus. Partner serostatus data were available for 4732 (71%); of these patients 2328 (49%) partners were HIV negative. Limited space and shortage of health staff has prevented full implementation of critical interventions

e.g, demonstration of correct condom use, risk reduction counseling, provision of family planning and STI services. Other challenges include stigma and disclosure of HIV status especially for female partners.

Conclusions: In 2008, partner HIV status was reported for 11% of HIV-TB patients of whom 49% were negative. This significant level of discordant partnerships underscores the need to expand the scope and quality of PwP services in clinical settings. Substantial resources to support infrastructure and manpower are needed.

FA-100725-13 Assessment of integration of TB services into antenatal Care-PMTCT services in KZN, South Africa

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Background: This study aims to assess the level of integration of TB into PMTCT services and identify barriers related to integration of TB into PMTCT services.

Methods: The study was conducted in one of the rural districts of KZN. Both quantitative and qualitative research methods were used. Routine data from 10 selected facilities in Sisonke district were collected and analysed. Exit interviews with pregnant women from same facilities were conducted and 26 key informants interviews (KIIs) were conducted with provincial, district and facility managers. Ethical clearance was obtained from the University of the Western Cape and the DOH-KZN research unit and written consent forms were signed by all participants.

Results: 150 antenatal care (ANC)-PMTCT clients were interviewed, 73% of participants reported that they were educated on TB symptoms by healthcare worker (HCW) on the day of the visit at the facility, 57% of them were screened for TB symptoms while 26% of the TB suspects were requested for sputum by HCW. From facility routine data, out of 1699 ANC clients, 1623 (96%) of them were tested for HIV and 542 (33%) of them were HIV positive. Out of 542 ANC clients who are HIV positive, 298 (55%) of them were screened for TB symptoms and no data was recorded for IPT. Qualitative results shows that the majority of program managers and coordinators at both provincial and district levels and facility managers felt that the integration of TB care into routine ANC/PMTCT services is happening but there are some barriers that impede full integration of TB care into PMTCT services. The most predominant barriers identified include lack of leadership, planning, trained HCWs, lack of supervision to ensure that guidelines are being implemented and weak referral system.

Conclusion: The findings of this study suggest integration of TB services into PMTCT will require strong leadership that will address managerial and operational barriers, reinforce supervision and training.

FA-100769-13   Peer educators' involvement in scaling up intensified TB case finding among persons living with HIV

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Background: The TB-HIV syndemic remains an important public health problem in Rwanda. Tuberculosis (TB) is a treatable disease but remains the leading cause of death among persons living with HIV (PLWH). In 2005, the Ministry of Health approved a national TB-HIV policy that includes screening all HIV-infected patients for active TB and linking all suspects to TB diagnosis and therapy. To respond, the International Center for AIDS Care and Treatment Programs (ICAP) in Rwanda integrated TB screening in the peer educator (PE) program.
Methods: Since 2008, ICAP has partnered with the Rwanda National Network of PLWH to enhance adherence, referral and linkages of patients enrolled in HIV care programs through peer education. By the end of 2009, 351 PE from 34 ICAP-supported facilities attended a participatory training, including TB screening, documentation of the results and referral. Each PE was assigned 30 families of PLWH who were visited monthly. Patients newly enrolled in the HIV program and their family members were screened for TB using the national 5-question TB screening checklist based on TB symptoms. Persons who screened positive were accompanied by the PE to the nearest health facility for a diagnostic work up and TB treatment if indicated.
Results: Between Jan. and Sept. 2009, 52 844 persons were screened for TB by the PE, 612 were identified as TB suspects and 64 were subsequently diagnosed with TB and initiated treatment. 21.6% (189/877) of all TB cases at ICAP-supported sites were detected through active case finding in PLWH. Of these, 33.9% (64/189) were detected by the PE. The likelihood that a person who screened positive for TB by a health care worker has TB is slightly higher than one screened by the PE (OR = 1.16). However, this difference is not statistically significant ($P = 0.40$; CI = 0.83–1.61).
Conclusion: PE, when adequately trained, can be as effective as health care workers in identifying potential TB cases amongst PLWH.

FA-100914-13   Preliminary findings from an isoniazid preventive therapy program in Viet Nam, 2008–2010

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Background: The World Health Organization recommends HIV-infected persons be screened for tuberculosis (TB) and evaluated for TB preventive therapy. In Viet Nam, an isoniazid preventive therapy (IPT) pilot program was implemented in two provinces and screening, enrollment and treatment were evaluated.
Methods: During April 2008–March 2010, HIV-infected persons in home-based care and HIV outpatient clinics were pre-screened for eligibility based on age (>15 years) and no TB history, alcohol abuse, or liver disease. Eligible persons were later screened for hepatitis, using liver function tests, and TB disease, using symptom screening, chest X-rays, and sputum smears. Isoniazid was administered for nine months. TB symptoms and adverse events were assessed monthly. Program records were reviewed and evaluated.
Results: Among 1401 HIV-infected persons, 1281 (91%) were pre-screened. Of 850 (66%) eligible persons, 520 (61%) were further screened, and 416 (80%) initiated IPT. During screening 17 people (3.3%) were diagnosed with TB and treated. Among persons on IPT, the mean age was 33 years, 210 (51%) were male, 147 (35%) unemployed, 199 (48%) on antiretroviral therapy, and 325 (78%) taking cotrimoxazole. During treatment, there were no severe adverse events reported. To date, 307 (74%) successfully completed IPT, 82 (20%) are still on treatment, and 28 (6%) did not complete treatment: 17 stopped IPT (15 defaulted, 2 physician's decision), 7 died and 3 developed TB.
Conclusions: In Viet Nam, over one-quarter of the target group started IPT, treatment completion was high and there were no serious complications. Scale-up of IPT is recommended.

FA-100961-13   Intensified TB case finding amongst HIV-positive clients using a standardized symptom screening tool

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Background: The TB incidence rate in South Africa is 948/100 000 with an HIV prevalence of 29%. It is

estimated that 73% of TB patients are co infected with HIV and TB has been reported as the number one cause of death in this population. Yet, less than 40% of HIV infected individuals are screened for TB.

Aim: To demonstrate that using a simple symptom screening tool to identify TB suspects will increase TB case detection amongst HIV positive clients and reduce the incidence of TB.

Methods: A standardized tool with 8 questions was developed by the TASC II TB project in 2007. The tool was administered by HIV counselors as well as nurses to HIV positive clients, in 212 facilities across 5 provinces supported by the project, from October 2007 to September 2009. The tool assessed whether the client had a cough, loss of appetite, weight loss, tiredness, night sweats, fever and lymph nodes. If any one of the symptoms was present, investigations to confirm TB were done and if found to have TB treatment was started immediately.

Results: The proportion of HIV positive clients screened in 2006/7, before implementation of the tool, ranged from 8% to 25%. The introduction of the tool increased this proportion to an average of 40% across the provinces. The incidence of TB cases reduced from 16 000 to 37 000/100 000 in 2006/7, down to 12 000 to 600/100 000.

Conclusion: The use of a symptom screening tool increased the number of HIV positive clients screened for TB and reduced the incidence of TB in these selected facilities. The early detection of TB using the tool also enabled possible interventions for co-infected patients which in the long term reduce morbidity from dual infection with TB and HIV.
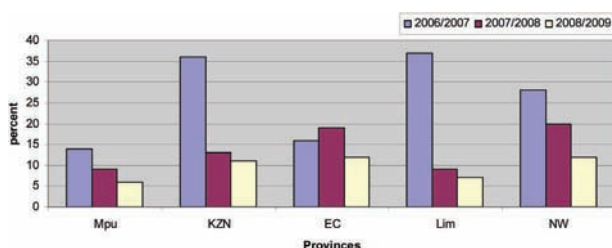
Figure   Percent HIV+ screened and found with active TB.

FA-101085-13   Does using a standardized TB screening tool improve TB control among PLHIV?

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Background: In 2008 ICAP supported Tanzania to roll out a 5-item TB Screening Questionnaire (TSQ) to increase TB case detection among patients attending HIV care/treatment clinics (CTC).

Methods: Review of 2 years routine CTC data on TB screening, suspects and notification prior to and after TSQ introduction (yr 1: Oct 07–Sep 08; yr 2 Oct 08–Sep 09). A random sample of HIV patient charts and related data from laboratory and radiology departments were assessed at 2 high volume hospitals.

Results: Over the 2 years, 28 947 PLHIV were enrolled at 91 ICAP-supported CTCs. Prior to the introduction of TSQ, 89% were screened for TB compared to 97% after the TSQ. Suspects identified increased from 9% in year 1 to 16% in year 2, but TB cases identified remained stable at 3%. An investigation into possible explanations for continued low TB notification showed: 1) 68% of TB suspects had no diagnostic process recorded in their CTC file; 2) only 16% of those with a recorded negative sputum had a CXR documented; 3) there was no evident increase in the proportion of patients at the TB clinic referred from CTC over the 2 years (36%); 4) among TB-HIV cases, updated TB treatment status was not recorded in 42% of patient CTC files; 5) laboratory records showed that patients giving sputum increased over 2 years (781 vs. 1096; 6) but the frequency of CXR examination did not increase over time.

Conclusions: The TSQ was associated with an increase in the proportion screened and suspected of TB, but the TB case rate remained stable. This may be explained by absent or incomplete diagnostic processes for TB suspects at CTCs, especially those who are sputum negative. Clinical record keeping of TB suspects and cases within the CTC is poor. Additional high volume sites will be investigated to evaluate current findings.

FA-100554-13   Practical interventions to improve TB case detection: experience from Ethiopia

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Background: Although Ethiopia has made significant progress in expanding DOTS services and improving TB treatment outcomes, low TB case detection has remained to be the key challenge facing TB control in the country. The World Health Organization (WHO) estimates, only 28% of smear positive TB patients were detected in 2007. The Ministry of Health is working with partners to improve the situation. In July 2008, TBCAP, a USAID supported TB project, started to implement a number of TB control activities in three zones namely North Shoa of Amhara, East Shoa of Oromiya and Gurage of the Southerrn Nations, Nationalities and Peoples Regional States. In January 2010, TBCAP was given another four new zones to support, namely, Arsi, West Arsi and West Shoa of Oromiya, and Awi of Amhara Regional States.

We assessed the trend of TB case detection in the three zones supported by TBCAP and the four new zones.

Methods: TBCAP support focused on: strengthening laboratory services, capacity building by training all health workers, providing equipment and supplies, and strengthening supervision, monitoring and evaluation. Data from TBCAP supported zones and the new zones were compared. The source of information was TB registers, forms and case notification reports.

Results: The TB case detection rate increased from 30% (2139/7130) in July 2008–June 2009, to 47% (482/1026) in July–Sept 09, and then to 64% (677/1026) in Oct–Dec 09 in TBCAP supported areas while there was no change in the TB case detection rate of 31% (4166/13 192) in the same period in the new zones that were not previously supported by TBCAP.

Conclusion and recommendations: TB case detection can be improved by strengthening TB control activities and working in partnership with all stakeholders. Lesson learnt from TBCAP supported areas should be documented and scaled-up to other parts of the country.

CLINICAL AND EPIDEMIOLOGICAL RESEARCH IN TUBERCULOSIS

FA-100216-13   Ag85B-ESAT-6 adjuvanted with IC31® promotes strong long-lived *Mycobacterium tuberculosis* specific

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Improved TB vaccines that induce long-term immunity against TB are urgently needed. Protective immunity against *Mycobacterium tuberculosis* is thought to depend on Th1-type cellular immune responses which leads to the secretion of IFN-γ. Here, we monitored safety and IFN-γ responses in healthy TB–naïve humans receiving a novel synthetic TB vaccine, composed of a defined antigen, fusion protein Ag85B-ESAT6 (H1), and IC31®, a new Th1-promoting adjuvant. The H1 fusion protein was tested in a phase I study in healthy male volunteers, administered at 0 and 2 months as recombinant protein alone or combined with two concentrations of IC31®. Safety was evaluated by physical examination and blood and urine parameters. Immunogenicity was monitored over a 2½ year period by detection of IFN-γ production by antigen-stimulated PBMC in response to the Ag85B-ESAT6 fusion protein or to peptide pools of each individual antigen using ELISpot, and ELISA. The effect of vaccination on the QUANTIferon® diagnostic test was also monitored. Vaccination did not cause local or systemic adverse effects besides transient soreness at the injection site directly after injection, but it elicited strong antigen specific T cell re-

sponses against H1, directed against both the Ag85B and ESAT6 components. Maximal responses were in the highest dose adjuvant group: against H1 this reached a median of 501 IFN-γ spot-forming cells per million PBMC and a median of 2833 pg IFN-γ/ml in supernatants of in vitro stimulated PBMC, for the group of vaccinated individuals. Remarkably, these strong responses persisted through 2½ years follow-up, indicating a substantial memory response in the vaccine recipients. In conclusion, the TB subunit vaccine Ag85B-ESAT6, given in combination with the novel adjuvant IC31® is safe and well-tolerated in healthy TB naïve volunteers and induced a strong Th1-type cellular immune response that persisted undiminished for 2½ years after vaccination.

FA-100210-13   Clinical trial of the efficacy of linezolid in XDR pulmonary tuberculosis

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Background: There are a growing number of patients not responding to any therapy who have little hope for survival without new drugs. Linezolid (LZD), an antimicrobial approved for gram positive bacterial infections, has been used off-label for drug resistant TB, despite lack of clinical evidence of efficacy.

Objectives: The primary objective of this study is to evaluate the efficacy of LZD treatment, as measured by sputum culture conversion in subjects that have failed to respond to anti-TB chemotherapy. This study was designed to mirror the way in which LZD is used clinically in salvage regimens for patients with chronic XDR disease and to understand how to maximize utility while minimizing toxicity.

Designs/methods: This is a Phase 2a, randomized, 2-arm study of LZD, which will be added to their existing regimens of enrollees at National Masan Tuberculosis Hospital in South Korea whose isolates have shown resistance to all known active TB drugs or who have failed to respond to any active drugs to which they are susceptible. This study involves two randomizations; first, subjects either immediately add 600 mg LZD once daily or delay for 2 months before starting LZD. Second, following sputum conversion subjects either continue 600 mg LZD qd or deescalate to 300 mg LZD qd. In total, 40 subjects will be accrued and randomized for the trial.

Results (preliminary): We enrolled 18 subjects in this study (11 non-diabetics/7 diabetics) including 4 that have withdrawn resulting in 14 subjects on trial by Jan 2010. Among them 10 subjects have achieved sputum smear and culture negative conversion. A total of 3 serious adverse events (SAEs) related to the study

drug have occurred including myelosuppression (anemia and neutropenia) in 2 subjects and peripheral neuropathy in 1 subject.

Conclusions: Linezolid could be an effective therapeutic option in untreatable MDR/XDR-TB. Its side effects remain a major limitation to use in long-term therapy.

FA-100073-13   Intensified TB case finding among HIV-negative TB suspects linked to a mobile VCT service, Cape Town

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Background: South Africa has one of the worst TB epidemics in the world (estimated incidence, 948/100 000). The DOTS strategy is insufficient for TB control in southern Africa and additional strategies such as intensified TB case finding (ICF) urgently need to be assessed.

Objectives: To assess feasibility of ICF in HIV-negative individuals accessing a mobile HIV testing service.

Methods: The study was conducted at a mobile HIV-testing service operating in underserviced communities in greater Cape Town in 2009. All HIV-negative adult TB suspects (cough >2 weeks, weight loss, fever, haemoptysis) were invited to participate. A questionnaire was completed and one induced sputum sample was sent for microscopy and culture. Participants with positive results were contacted for referral to their local TB treatment clinic.

Results: 163 of 165 eligible individuals participated. The median age was 39 years, 57% were males and 70% were black. Only 41 (26%) individuals had previously sought medical care for their symptoms and just 14 had undergone TB investigations. Sputum samples were obtained from 147 (91%) individuals; 15 were unable to produce a sample and one individual refused sputum induction. TB was diagnosed in 11 individuals (3 smear-positive/culture-positive, 8 smear-negative/culture-positive). Overall TB prevalence was 7.5% (95%CI 3.8–13.1). All but one individual were successfully contacted.

Conclusion: The uptake of ICF was high when offered to individuals attending a mobile VCT service. The yield among HIV-negative symptomatic individuals was 7.5% with most being smear-negative/culture-positive. Linkage to care was successful in most cases. This strategy may enhance TB control in high prevalence settings.

FA-101262-13   Malawian patients at risk of death during TB treatment are identified by basic clinical observations

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Introduction: Up to 20% of Malawian adults die during TB treatment; most deaths occur during the 2 month intensive phase. Easily identifiable factors predisposing to poor outcome may allow trials of adjunctive treatment strategies or closer clinical monitoring in high risk patients. This would be of great value in settings such as Malawi where a human resource shortage in the health sector allows little time for detailed clinical assessment.

Table   Univariate analysis of risk factors for clinical deterioration during the intensive phase of TB treatment

Variable	Odds ratio	95%CI	P value
Clinical examination			
Performance status (0–4)	1.60	0.98–2.61	0.07
Reduced body mass index (BMI) (kg/m²)	1.53	1.19–1.96	<0.001*
Temperature (°C)	0.92	0.64–1.34	0.68
Reduced O$_2$ saturations (%)	1.11	1.02–1.22	0.01*
Respiratory rate (breaths/min)	1.13	1.03–1.23	0.01*
Number of zones affected clinically	1.11	0.85–1.46	0.45
Bilateral chest signs	1.97	0.66–5.91	0.24
Pulse (beats/min)²	1.02	1.00–1.05	0.04*
Reduced systolic blood pressure (mmHg)	1.05	1.00–1.10	0.04*
Disorientation (0 to 3: time, place or person)	2.31	0.89–6.01	0.10
Baseline investigations			
Reduced haemoglobin (g/dl)	1.36	1.06–1.73	0.01*
Total white cell count (10⁹/l)	0.84	0.67–1.06	0.10
Monocyte count (10⁹/l)	0.91	0.34–2.42	0.85
Reduced platelet count (10⁹/l)	1.00	1.00–1.01	0.01*
CD4 < 200 (HIV positive patients only)¹	3.67	0.98–13.70	0.03*
Sputum smear negative	1.80	0.68–4.80	0.26
Elevated ALT or Bili	2.30	0.59–9.03	0.26
Elevated urea or creatinine	4.78	1.45–15.72	0.02*
Number of zones involved on CXR	1.33	0.93–1.90	0.10
CXR changes 'atypical' for TB	1.01	0.35–2.88	0.99

Aim: To evaluate risk factors for death or clinical deterioration ('poor outcome') during the two month intensive phase of TB treatment.

Methods: A prospective cohort of 202 patients commencing treatment for culture proven pulmonary TB at Queen Elizabeth Central Hospital, Blantyre, Malawi. Detailed history emphasising demographic, socioeconomic and medical factors and clinical examination was conducted by an experienced middle grade

physician. Analysis compared those with poor outcome (cases) with those who had an uncomplicated clinical course (controls).

Results: 12 (6%) died and 10 (5.5%) had a severe clinical deterioration which responded to intervention. Univariate associations are shown in the Table, with independent predictors of poor outcome being low BMI (OR 1.44 (1.11–1.86)) and high respiratory rate (OR 1.12 (1.02–1.23)). The rule (0.1*resp-0.4*BMI) > −5.35 has 72.2% sensitivity and 70.9% specificity (PPV = 21.3% and NPV = 95.9%) in classifying patients at risk of deterioration. Detailed evaluation by an experienced clinician yielded no additional benefit in predicting high risk patients.

Conclusion: Identification of patients at risk of death during the intensive phase of TB treatment in resource poor settings such as Malawi should focus on simple, objectively measurable parameters such as respiratory rate, BMI, pulse and blood pressure. Our classification rule should be tested in a validation cohort, and should enable intensified follow-up of those at high risk, with potential for referral to a higher level of healthcare.

FA-101433-13   Frequency and clinical outcome of patients with mixed *Mycobacterium tuberculosis* infections

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Background: Recent studies have highlighted the frequent isolation of several *Mycobacterium tuberculosis* strain lineages in single disease episodes, often with differing drug susceptibilities. However, an understanding of the nature and frequency of mixed infections is lacking. This study investigated the frequency of mixed TB infections in the Delft region of the Western Cape, as part of a clinical trial on the effects of micronutrient supplementation together with standard TB treatment.

Methods: Newly diagnosed, adult TB patients (*n* = 154) enrolled in the trial, provided a single weekly sputum sample over an 8-week period. Spoligotyping was used to detect mixed infections and to assess the epidemiology of *M. tuberculosis* in the serial *M. tuberculosis* isolates isolated from the TB patients (*n* = 686). Strain-specific PCR assays were undertaken to

detect infections by W-Beijing and non-W-Beijing isolates, as well as to differentiate between mixed non-W-Beijing isolates. Phenotypic and genotypic drug susceptibility testing (DST) was also undertaken.

Results: Spoligotyping indicated that W-Beijing isolates constituted a large proportion (47.8%) of *M. tuberculosis* in this region, with other strains detected including LAM (17.1%) and T (14.7%). Mixed infections were detected in 27 (21%) of 129 patients screened. DST confirmed that all isolates identified in patients harbouring mixed strains by spoligotyping were fully susceptible to both rifampicin and isonaizid. Of the 27 patients harbouring mixed infections, sputum from 20 (74%) remained culture positive at week 8. Supplementation with vitamin A and zinc appeared to have no effect on the frequency of mixed infections in the treatment group (23%) as compared with the placebo group (30%).

Conclusion: The high frequency of mixed infections in this area warrants further attention and may have implications with regard to the interpretation of epidemiological and DST data, and the subsequent treatment of patients.

FA-101202-13   Incidence of child tuberculosis among household contacts of all types of TB patients: a 4-year study

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Background: TB remains a major cause of death and disability across the globe. Pakistan ranks 8th most high TB burden country in the world. The National TB control Program relies heavily on self reporting by the patient, which at times result in delayed diagnosis or mismanagement. Due to the infectious nature of the disease, it tends to spread in close proximity. Immediate household contacts of all types of TB patients specially sputum positive, remained very vulnerable to carry TB infection or develop the disease among the children.

Methodology: A 4-year (2006–2009) data analysis was done of all types of TB patients diagnosed by Marie Adelaide Leprosy Centre in Karachi. All immediate household contacts were examined at least twice (at the time of registration and discharge) for

	2006	2007	2008	2009
TB patients diagnosed, all types *n*	582	577	640	838
Contacts examined, *n*	4387	3889	3720	5251
New cases detected among contacts, *n*	63 (1.43%)	87 (1.43%)	81 (2.1%)	134 (2.55%)
Child TB cases detected among household contacts	22 (0.5%)	10 (0.25%)	14 (0.37%)	34 (0.64%)

the cardinal signs and symptoms of the disease and below number of children detected for TB.

Conclusion: TB incidence in Pakistan is 181/100 000 (0.181%). Household contact examination of all types of TB patients has revealed that the incidence of child TB is 0.25–0.64 and the mean is 0.44 = 440/100 000 which is quite high which needs to be addressed by doing contact screening for early detection, treatment and disrupt the transmission cycle among the children.

FA-101322-13   Patient-provider interaction: the key to reducing default, irregularity and stigma

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Introduction: Sahyog project of LEPRA Society is an EU and LEPRA UK supported project to strengthen the health system in order to reduce tribal vulnerability to TB and HIV/AIDS. The project is being implemented in 3 tribal districts of Orissa, India. Irregularity in treatment, issues of default and less cure and conversion are some of the major issues in tribal districts of Orissa. Therefore the project to address such issues facilitates patient-provider interaction circuit in the periphery health institute.

Objective: To analyze the effect of patient-provider interaction in TB management in high case load tribal areas of Orissa, India.

Methodology: In 2009 the project conducted 65 patient provider interactions in which service providers, patients, family members and project staff participated. The results of those circuits are analysed.

Major findings: The project organised 65 TB interaction circuits at field level where 1778 persons including 808 TB patients (502 M and 306 F), 563 DPs (88-M 475-F) and 407 family members participated. All TB cases were counseled, their treatment card and medicines were verified. As a result, 12 defaulter cases retrieved, 48 irregular cases regularised, 74 follow-up sputum collected at the interaction point, 374 TB cases referred for HIV testing. 306 TB cases got HIV tested and 2 among them found HIV positive. Patients having other complications/complaints provided with medicines under the guidance of the Medical officers attended.

Conclusion: Patient-provider interaction in tribal and high case load areas found be one of the key strategies to be adopted in TB control measures to reduce the defaulter and thereby could also prevent MDR. This also increases participation of family members and community leaders which reduces stigma considerably along with food/nutrition support to needy persons. It seems to be a key contributor to follow-up sputum collection and testing and propagating the same in the community.

FA-101256-13   Survival of smear-negative pulmonary TB patients in the United States, 1993–2005

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Background: Data from resource-limited countries demonstrate that people with HIV who have sputum-smear negative TB (SnTB) are at increased risk of death compared to those with sputum-smear positive TB (SpTB). We sought to describe the influence of sputum-smear status on survival in people with HIV diagnosed with TB in the United States.

Methods: We analyzed data for all people with reported, culture-confirmed pulmonary TB with HIV in the United States from 1993 to 2005, comparing characteristics of patients with SnTB to those with SpTB. Kaplan Meier plots and log rank tests were used for bivariate comparisons and Cox proportional hazard ratios, adjusting for age, race/ethnicity, nationality, correctional institution residence, and drug and alcohol use, were used for multivariate analysis. Analyses were stratified by availability of highly active anti-retroviral therapy (HAART), with 1997 and prior defined as pre-HAART and 1998 and beyond defined as the HAART era.

Results: Characteristics of patients with SnTB and SpTB disease were similar. The survival curves stratified by sputum-smear result were significantly different, in both the pre-HAART and HAART eras (log rank statistic = 22.7, $P < 0.0001$; log rank = 9.2, $P = 0.002$, respectively). On Cox proportional hazard analysis, SnTB patients had decreased risk for death (HR 0.82, 95%CI 0.76–0.88; HR 0.83, 95%CI 0.73–0.93, for pre-HAART and HAART eras respectively).

Conclusion: In the United States, people who had SnTB in both pre-HAART and HAART eras had better survival compared to those with SpTB, suggesting that SnTB in people with HIV does not represent more severe illness. Misdiagnosis and treatment delays may contribute to the decreased survival in patients with SnTB disease in resource-limited countries, supporting the urgent need for scale-up of better diagnostic technologies.

FA-101374-13   Risk factors for death in TB patients in the European Union: analysis of case-based data

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Background: The 30 countries of the European Union (EU), EEA and EFTA present a wide spectrum of epidemiological patterns of TB. A study of risk for death

among TB patients could better target public health interventions.

Intervention: Harmonized national surveillance data on TB have been collected for 15 years in case-based format. This information, now coordinated by ECDC, allows an analysis for risk factors for death with adjustment for other covariates. Random effects logistic regression (adjusting for clustering at country level) was used to study the association between risk factors and death from any cause. Data were pooled for 2005–6 without adjustment for time effects. The risk factors investigated were age, sex, origin, site of TB, previous TB history, and multidrug resistance (resistance to both isoniazid and rifampicin; MDR). Strength of association was expressed in adjusted odds ratios and their 95% confidence limits.

Table Associations between different risk factors and death among TB patients, 14 countries, 2005–2006

Risk factor	OR	95% CLs	*P* value
Age 0–19 yrs	1.0	Ref.	
Age 20–39 yrs	4.10	1.92–8.75	
Age 40–59 yrs	11.07	5.22–23.47	<0.0001
Age 60+ yrs	38.15	18.03–80.69	
Male vs. female	1.30	1.16–1.45	<0.0001
Foreign vs. local origin	0.52	0.45–0.61	<0.0001
Pulmonary vs. extra-pulmonary site	1.44	1.22–1.71	<0.0001
Previously diagnosed vs. not previously diagnosed	1.15	1.09–1.22	<0.0001
MDR vs. not MDR	4.28	3.63–5.03	<0.0001

Results: 19 309 TB cases with full data were reported by 14 EU/EEA/EFTA countries in 2005–6 (Cyprus, Czech Rep, Estonia, Germany, Iceland, Ireland, Latvia, Lithuania, Netherlands, Norway, Portugal, Slovenia, Slovakia, UK). The proportion of MDR among all cases was 6% (country range: 0–18%) and 11% (3–15%) died. Risk for death from any cause increased markedly with advancing age and with the presence of MDR (Table). The inter-country correlation coefficient of the null model for variability in proportion of death was measured (rho = 0.06). The risk factors in the model explain a large part of this variability (rho = 0.03; likelihood ratio test of rho = 0, $P < 0.0001$).

Conclusions: Incomplete geographical coverage of data and the absence of variables on important determinants (e.g. HIV status and alcohol dependency) preclude a more complete study. Nonetheless it is clear that drug resistance is an important risk for death among TB patients even in developed countries. Clustering effect is important to adjust for in such analyses.

FA-100297-13   Tuberculosis control in highly endemic prisons: impact of X-ray at entry and mass screening

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Background: Tuberculosis (TB) is highly prevalent in prisons of high and median endemicity countries. Based on a mathematical model, the combination of basic control methods (passive detection and treatment) with X-ray screening at entry in prison and X-ray mass screening was considered the most effective strategy to rapidly reduce TB prevalence. We report the evaluation of the impact of this strategy in a highly endemic prison.

Methods: We followed up for 2 years a Rio de Janeiro State prison for adult males. Detainees were screened by X-ray at entry and X-ray mass screenings were performed when the study was started and after one year. Sputum smear examination and culture were realized in detainees presenting with any X-ray abnormality or attending the prison dispensary for a cough ⩾ 3 weeks.

Results: A total of 4326 X-rays were performed and 246 TB cases were identified. TB prevalences among detainees screened at entry during the 1st and the 2nd year of the study remained similar: 2.8% (21/754) versus 2.9% (28/954) respectively, whereas prevalences decreased from 6.0% (83/1274) to 2.8% (35/1244) between the 1st and 2nd mass screenings ($P < 0.0001$). The incidence rate of cases identified in response to the spontaneous demand of detainees (i.e., independently of X-ray screenings) decreased from 4206 to 1926/100 000 between the 1st and the 2nd year ($P < 0.0001$). Overall incidence rates taking into account all cases identified through mass screenings and response to the spontaneous demand decreased from 9970 to 4823/100 000 between the 1st and the 2nd year ($P < 0.0001$).

Conclusions: The TB control strategy investigated, which was highly effective and well accepted by the detainees, should be considered in the context of highly endemic confined settings such as prisons.

POSTER DISCUSSION SESSIONS

DIAGNOSIS: SCREENING OF TB-HIV

PC-100223-13   Diagnosis of latent tuberculosis infection among HIV-infected persons

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Background: Patients co-infected with HIV and tuberculosis (TB) are at great risk of developing active TB. The sensitivity of tuberculin skin test (TST) may be reduced by HIV infection. There is also cross-reactivity with BCG and non-tuberculous mycobacteria. BCG vaccination coverage is very high in Hong Kong.
Method: T-Spot.TB (T-Spot), QuantiFERON-TB Gold-In Tube (QFT) and TST were compared among HIV-infected subjects attending an HIV clinic in Hong Kong. The results were correlated with their BCG vaccination and HIV disease status.
Results: Of 103 HIV-infected subjects successfully recruited from 1 Dec 2006 to 31 August 2010, 89 (86.4%) were males, and 64 (62.1%) had a BCG scar. The mean age was 42.9 (SD:10.7) years. The median CD4 count and viral load were 397 (range: 99–1106) and 75 (range: <50–399 830) per ml. None of them had previous history of TB. The positive rates for TST (5 mm cutoff), T-Spot and QFT were 8/102 (7.8%), 6/100 (6.0%) and 5/103 (4.9%) respectively. No significant difference was found in the test positive rates (McNemar test, all $P > 0.05$). The combined positive rate for all three tests was 17/103 (16.5%), which was closer to the estimated background infection prevalence of 20% at an annual infection risk of 0.5%. Agreement was poor between all three tests with kappa of 0.23 (TST vs. T-Spot), −0.64 (TST vs. QFT), and −0.05 (T-Spot vs. QFT). None of the tests were significantly associated with sex, age, BCG scar, CD4 count or viral load.
Conclusion: T-Spot and QFT did not perform better than TST among HIV-infected subjects despite a high BCG coverage. With their low positive rates and poor agreement, all three tests appeared to have limited sensitivity among this important target group.

PC-100580-13   Evaluation of the World Health Organization algorithm for the diagnosis of sputum smear-negative tuberculosis

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Background: In 2006 the World Health Organization (WHO) published recommendations to facilitate the diagnosis of a variety of forms of smear-negative tuberculosis (SNTB) in resource-constrained high HIV prevalence settings. We evaluated the diagnostic performance and outcomes of the WHO algorithm for the diagnosis of tuberculosis in ambulatory HIV-infected patients (or patients with unknown HIV status).
Methods: We applied the WHO algorithm to a cohort of ambulatory adult tuberculosis suspects with two negative sputum smears or inability to produce sputum attending primary care clinics in KwaZulu-Natal, South Africa. Induced sputum and other relevant specimens were sent for mycobacterial culture. Participants fulfilling WHO criteria for SNTB started antitubercular treatment, the rest of the cohort was observed, and all were followed up for 8 weeks. Confirmed tuberculosis was defined as positive culture or granulomata plus acid fast bacilli on histology.
Results: Two hundred and twenty one participants fulfilled the WHO ambulatory SNTB algorithm entry criteria of cough for >2 weeks, no danger signs, and HIV seropositive or status unknown. The diagnostic performance of the WHO algorithm was: positive predictive value 0.34 [95%CI 0.26–0.43]; negative predictive value 0.86 [95%CI 0.76–0.92]; positive likelihood ratio 1.44 [95%CI]; negative likelihood ratio 0.46 [95%CI]; and diagnostic odds 3.1 [95%CI 1.52–6.34]. Losses to follow up (4), hospitalizations (6) and deaths (5) did not differ significantly in those who were and were not diagnosed with SNTB.
Conclusions: The WHO ambulatory SNTB algorithm had a reasonably high negative predictive value but low positive predictive value. Applying the algorithm was associated with a low mortality over an eight week period.

PC-100582-13   Performance of C-reactive protein as a screening test for smear-negative tuberculosis in a high HIV burden setting

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Background: Tuberculosis is a leading cause of morbidity and mortality in sub-Saharan Africa, in part due to the high incidence of sputum smear-negative tuberculosis (SNTB) in high HIV prevalence countries. C-reactive protein (CRP) is a non-specific inflammatory marker that has been shown to be elevated in HIV-infected tuberculosis patients.

Methods: We evaluated the performance of CRP as a screening test for SNTB in the evaluation of 312 ambulatory SNTB suspects with cough for >2 weeks and seropositive and unknown HIV status in KwaZulu-Natal, South Africa. Participants were evaluated for SNTB, at least two specimens including induced sputum were sent for mycobacterial culture, and venous blood was taken for CRP measurement. Participants with evidence of SNTB were started on antitubercular therapy, and the rest observed. Confirmed tuberculosis was defined as a positive culture for *M. tuberculosis* or acid-fast bacilli with granuloma, and possible tuberculosis as evidence of SNTB with response to therapy. The CRP quotient was defined as the CRP result divided by the upper limit of normal for the assay.

Results: One hundred and fourteen (36.5%) participants were diagnosed with confirmed tuberculosis, 101 (31.1%) with possible tuberculosis and 97 (31.1%) did not have tuberculosis. The median CRP quotient and interquartile range (IQR) in these three groups was 15.9 (8.9 23.4), 5.8 (1.4 13.5) and 0.7 (0.3 2.5) respectively. A CRP quotient of >1 detected 88% tuberculosis cases (95%CI 83% 93%), with odds ratio 10.8 (95%CI 6.0 19.3), positive predicative value 0.83 (95%CI 0.77 0.87) and negative predicative value 0.69 (0.58 0.79). Specificity and positive predicative value increased as the CRP quotient increased (Table).

Table   Performance of CRP as a screening test for confirmed or possible tuberculosis in 312 HIV seropositive or status-unknown participants with cough >2 weeks

CRP quotient	Sensitivity (95% CI)	Specificity (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)	Odds ratio (95% CI)	Positive predictive value (95% CI)	Negative predictive value (95% CI)
>1 × ULN	0.88 (0.83–0.92)	0.59 (0.48–0.69)	2.14	0.20	10.8 (6.0–19.3)	0.83 (0.77–0.87)	0.69 (0.58–0.79)
≥ 2.5 × ULN	0.80 (0.74–0.85)	0.75 (0.65–0.83)	3.23	0.27	12.2 (6.9–21.5)	0.88 (0.82–0.92)	0.62 (0.53–0.72)
≥5 × ULN	0.72 (0.66–0.78)	0.83 (0.75–0.90)	4.37	0.33	13.1 (7.1–24.1)	0.91 (0.85–0.95)	0.57 (0.49–0.66)
≥10 × ULN	0.53 (0.46–0.60)	0.92 (0.84–0.96)	6.43	0.51	12.5 (5.8–27.1)	0.93 (0.87–0.97)	0.47 (0.40–0.64)

Conclusions: An elevated CRP quotient detected most cases of tuberculosis. CRP may be useful in improving diagnostic accuracy for SNTB and should be evaluated as a diagnostic tool in resource-limited settings.

PC-100592-13   Ability to diagnose tuberculosis in HIV-infected patients with symptoms of lung disease

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Setting: Differential diagnosis of pulmonary pathology in HIV-infected patients is quite difficult. This is often due to lack of typical clinical and radiographic manifestations of tuberculous process, and the negative result of sputum research on causative TB agent (MBT) with Ziehl-Neelsen stain.

Aim: Enhanced efficiency the laboratory diagnosis of tuberculosis in HIV-infected patients with symptoms of pulmonary disease.

Methods: Were examined in 37 patients with HIV infection with the presence of clinical and radiographic manifestations of pulmonary disease and the difficulties in obtaining the diagnosis. In the first place to patients was excluded tuberculous etiology of the process. To search for DNA MBT in the sputum used method of Real-Time polymerase chain reaction (Real-Time PCR) by a special DNA-amplificator with the optical block (iCycler Q), the company BioRad (USA). The procedure combines the stages of amplification and detection results of the reaction. Parallel in the patients three-fold investigated by sputum of indirect bacterioscopy with Ziehl-Neelsen stain.

Results: Active TB on the basis of aggregate data the epidemic anamnesis, clinical and radiographic manifestations, laboratory examination and Mantoux test was diagnosed in 35 patients, the two patients were diagnosed with community-acquired pneumonia. In all 35 patients with pulmonary tuberculosis registered positive sputum smear using PCR. Repeated sputum smear examination with Ziehl-Neelsen stain yielded positive results in only three cases (8.6%) in patients with signs of decay in the lung tissue. Therapy of tuberculosis led to clinical effect after 3 months of treatment in 26 patients (74.3%).

Conclusions: In patients with HIV infection with the difficulties of differential diagnosis of lung diseases Real-Time PCR greatly improves and accelerates the detection of tuberculous etiology of pathological changes.

PC-100757-13   A prospective audit of diagnostic laparoscopy in the diagnosis of abdominal tuberculosis

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Introduction: HIV/AIDS has resulted in a resurgence of abdominal tuberculosis in South Africa. The role

of laparoscopy in making the diagnosis is undefined. This prospective study looks at the role of laparoscopy in establishing the diagnosis of abdominal tuberculosis (TB).

Method: All patients with clinically and radiologically suspected but histologically or microbiologically unconfirmed abdominal TB were referred to the investigating team for laparoscopy. All grossly pathological tissues and free fluid were sent for histology and microbiological assessment.

Results: From January 2008 to January 2010, 118 patients were evaluated. Forty-two patients required emergency laparotomy either for bowel obstruction or peritonitis. All 42 patients had positive histology for TB and 13 of them demised (31%) post laparotomy. Seventy-six patients underwent diagnostic laparoscopy and 64 of them were HIV positive. Laparoscopic findings included intra-abdominal lymphadenopathy in 53, minimal ascitic fluid in 51, intra abdominal mass in 13, deposits on bowel wall, peritoneum or omentum in 15 patients. In 10 patients (13.15%) an alternative diagnosis was found (appendicitis, adenocarcinoma, lymphoma). Forty-nine patients (64.47%) had positive histology for TB. In 17 patients (22.36%) histology revealed non-specific inflammation and reactive lymph nodes. Fourteen of 15 deposits (93%) were culture positive. The masses biopsied were positive in 85% (11/13) of cases and the lymph nodes were positive in 68% (36/53) of cases. Ascitic fluid culture was positive in 35% (8/23) cases.

Conclusion: Laparotomy is an effective way of diagnosing abdominal TB but is associated with significant morbidity and mortality. Laparoscopy is very useful to diagnose alternate surgical pathology. Histology obtained at laparoscopy confirmed the presence of TB in 65% of cases.

PC-100765-13   Diagnostic yield of sputum induction among TB suspects assessed under routine conditions at a hospital

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Background and objective: The yield of smear microscopy among tuberculosis (TB) suspects is low where HIV prevalence is high. Sputum induction improves the yield, but its value in routine, non-research settings is unstudied. We assessed the yield of induced sputum (IS) for acid fast bacilli (AFB) on smear microscopy and culture for *M. tuberculosis*.

Methods: Retrospective analysis of 2802 patients at TB focal point at Helen Joseph Hospital, Johannes-

burg, South Africa, between October 2008–December 2009.

Results: Sputum collection was attempted in 2747 (98%) patients. Spontaneous sputum collection was successful in 1489 (54.2%). Among the other 1285 patients, IS was successful in 24.2%, failed in 62.8%, not tried because the patient was too ill (10.4%), because of time constraints (1.4%), or unspecified reason (1.2%). Among 1285 patients, 87.3% were HIV-positive (median CD4 count of 80 cells/mm^{3}). HIV was not associated with failure of IS if attempted (OR 1.28; 95%CI 0.85–1.93), but HIV-infected patients were more likely to be too ill for IS (OR 5.0; 95%CI 1.5–16.1). Smear microscopy was positive for AFB in 46.1% and 46.5% of spontaneous and IS samples, respectively. Among TB suspects without AFB on smear microscopy, liquid culture was performed on 315 sputum samples, of which 41.1% spontaneously collected sputum and 36.1% of IS samples were *M. tuberculosis* positive. Contamination rate was 10.9% for spontaneously collected sputum and 7.4% for IS. Sputum induction resulted in the diagnosis of 135 smear positive TB cases and 35 smear-negative, culture-positive TB cases.

Conclusion: Sputum induction improved the diagnostic yield for AFB and *M. tuberculosis* culture. Among 1285 patients, IS was successful in 24.2% and resulted in culture confirmation of TB in 170 (13.2%) patients unable to expectorate spontaneously.

PC-100819-13   Tracing patients with smear-negative TB lost to follow-up during the diagnostic process in Zimbabwe

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Background: Médecins Sans Frontières provides a TB and HIV outpatient service in Epworth, an informal settlement near Harare. Roughly 80% of TB patients are co-infected with HIV. More than 100 patients are screened for TB a month, 10–20% of whom do not return for results. All smear positive patients who do not return are traced to commence TB treatment. We examined the outcomes of tracing high-risk smear negative TB suspects who were lost to follow up.

Methods: Between November 2009 and February 2010, all smear negative TB suspects were assessed on 3 criteria: respiratory symptoms (productive cough, chest pain, dyspnoea and haemoptysis), systemic symptoms (fever, night sweats and weight loss) and TB contact history, with each criterion graded from 0 to 2. Smear negative suspects not completing the full TB diagnostic work-up (2 sputum smears, course of broad spectrum antibiotics, chest X-ray and review by physician) by not returning for results within

a week of initial consultation were classified as lost to diagnostic follow-up (LDFs). LDFs were classed as high risk if they scored 2 or more on clinical and epidemiological grading. All high-risk smear negative LDFs were traced by community workers and if still unwell completed the diagnostic work-up.

Results: There were 53 high-risk LDFs—16% of all patients screened for TB in the outpatient department—all of whom were traced and completed the diagnostic work-up. Of these, 40 (75%) were diagnosed with TB. 73 patients were diagnosed with smear negative TB during this period, of whom 59 (81%) were HIV positive.

Conclusions: A high proportion of smear negative patients lost to follow up during routine diagnostic work-up can be traced and subsequently shown to have TB. Patients with smear negative TB in high HIV endemic regions have higher mortality rates than those with smear positive TB. Improving services to minimise loss to follow up during the TB diagnostic work-up is vital to ensure early diagnosis and treatment.

PC-101315-13 Assessment of new strategies for diagnosis of TB-HIV co-infected patients in Cotonou, Benin

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Background: In tuberculosis (TB) endemic and low resource countries, diagnosis of TB is still mainly based only on classical microscopy. However, the sensitivity of this test is reported to be low on HIV-infected patients. In many of these countries, HIV therapy is now available but strategies to diagnose HIV-infected patients are not always adequate.

Setting: The national pneumo-phtisiology hospital, where about one-third of all TB patients from Benin are diagnosed every year.

Objective: To determine the usefulness of new tools and/or strategies for the diagnosis of HIV and TB. These tools were systematic HIV testing on patients with chronic cough, LED fluorescence microscopy after bleach concentration of sputum and home-made liquid culture.

Methods: All 756 patients with age above 15, consecutively admitted in the hospital from May to October 2009, for chronic cough are included in the study. All patients were tested for HIV after counseling. For HIV-infected patients, CD4 count and viral load were measured. For all patients, sputum samples were subjected to direct LED fluorescence microscopy, LED fluorescence microscopy after bleach concentration, culture using a home-made 7H9 liquid medium and a home-made Löwenstein-Jensen solid medium.

Results: HIV prevalence in patients confirmed of having TB (19%) was higher than that of patients who

were not confirmed of having TB after microscopy and culture (30%) ($P < 0.001$). Bleach concentration method lead to an incremental yield of 7.5% positivity in all patients but 53% in HIV-infected patients. The positivity rate in liquid culture was also higher in HIV-infected patients than that of HIV-non infected patients.

Conclusion: HIV serology lead to a detection of more HIV-infected patients and should be recommended for all patients with chronic cough, not only TB patients. Bleach method as well as home-made liquid culture improved the diagnosis of TB in HIV-infected patients. These methods would be useful in our setting.

PC-101345-13 Tuberculosis screening practices among patients enrolled into HIV care in Lusaka, Zambia

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Background: Current WHO guidelines require TB screening in HIV-infected patients with cough greater than 2 weeks duration, while anticipated guidelines will advocate screening in patients presenting with any current TB-related symptom. We compared the number of patients requiring screening with existing guidelines with the additional burden posed by new guidelines.

Methods: A retrospective chart review was performed on all new enrollees to HIV care at a primary care clinic in Lusaka. Patients presenting with at least one current TB symptom (cough, night sweats, fever, weight loss, hemoptysis, or loss of appetite) between June and December 2009 were selected. Demographic data, TB symptoms, diagnostic tests (microscopy/chest radiography) and diagnostic outcomes were recorded. A descriptive analysis was performed.

Results: Chart review included 154 symptomatic patients. Their median age was 34 years, 51% were female, 72% were WHO stage III or IV, their median body mass index was 19, and their median CD4 count was 106. Any cough was documented in 138 (90%) of these 154 patients, and 84 (61%) had documented cough > 2 weeks. Of patients with >2 weeks of cough, TB screening was initiated in 49 (58%).

Conclusions: Present screening guidelines are not consistently followed as evidenced by just over half of eligible patients undergoing screening. Implementing anticipated WHO guidelines based on existing screening practices will increase the screening workload by approximately three-fold. Successful implementation of new intensified case finding guidelines will require significant commitment of additional resources, staff and training.

TB-HIV EPIDEMIOLOGY: CLINICAL RESEARCH/TREATMENT/CARE

PC-100775-13   High rates of unmasking TB IRIS and ART treatment failure among individuals on ART diagnosed with TB

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Background and objective: Antiretroviral treatment (ART) reduces the risk of HIV-associated tuberculosis (TB), but high rates of 'unmasking' TB immune reconstitution inflammatory syndrome (IRIS) can occur in the first months of ART. We assessed the characteristics of patients diagnosed with TB by duration of ART.
Methods: Retrospective analysis of patients presenting to the TB focal point of the Helen Joseph between October 2008 and December 2009.
Results: Among 2318 HIV-positive patients, 379 (16.3%) were on ART at time of TB diagnosis. TB treatment and ART initiation dates were available in 364 (96%) patients. Unmasking TB IRIS (first 3 months of ART) occurred in 176 (48.3%) patients, after a median of 32 days on ART (IQR 16–57). Incident TB occurred in 188 (51.7%) patients, after 3 months to 6 years of ART. CD4 count was lower in IRIS than non-IRIS cases (74 vs. 149, $P < 0.001$). Pulmonary involvement was present in half of both IRIS cases and non-IRIS cases (54.5 and 50.5%), but IRIS cases were less likely to have smear-positive TB (37.5% vs. 51.6%, $P = 0.045$). Lymph node TB was diagnosed in 12.6 and 9.0% of IRIS and non-IRIS cases, pleural TB in 14.7 and 21.8%, miliary TB in 7.3 and 3.7%, abdominal TB in 23.8 and 15.9%, and CNS TB in 6.3 and 8.5% (all $P > 0.05$). VL data was available in 86 (62.8%) patients on ART for $\geqslant$6 months, 19.8% had a VL > 500 copies/ml.
Conclusion: Almost half of all individuals on ART hospitalized for TB were cases of unmasking TB IRIS, diagnosed within the first 3 months of ART. TB-IRIS cases were more likely to have smear-negative TB, tended to be more likely to have disseminated forms of TB, including abdominal or miliary TB, and tended to be less likely to have pleural TB. One in five non-IRIS TB cases occurred in individuals failing ART prior to developing active TB. Improved screening for TB at ART initiation, optimal ART adherence and timely initiation of second line ART are needed to reduce the burden of ART-associated TB.

PC-100142-13   Uptake and predictors of acceptance of HIV testing among suspects of tuberculosis in Addis Ababa, Ethiopia

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Background: The World Health Organization recommended that TB suspects should be screened for HIV. However, little is known about the acceptance rate of HIV testing among TB suspects in Ethiopia. The objective of this study was to assess the uptake of HIV testing among TB suspects in Addis Ababa, Ethiopia and to determine reasons for non-acceptance of the test.
Design: From February to March 2009, new TB suspects, identified in 27 health centers in Addis Ababa were proposed to be tested for HIV. Patients were interviewed by trained nurses using a pretested questionnaire.
Result: Of the 506 TB suspects, 59% were tested for HIV and accepted the test result. Individuals knowledgeable on the HIV counseling and testing procedures were 2.5 times more likely to be tested than individual who had poor knowledge. TB suspects who had previously been tested for HIV were 2 times more likely to accept HIV testing and to receive the result of the test [OR = 2.0, (95%CI: 1.4, 2.9)]. Government employees [OR = 2.8, 95%CI: 1.2, 6.3)] and merchants [OR = 2.7, (95%CI: 1.2, 5.7)] were more likely to be tested for HIV as compared to jobless individuals.
Conclusion: The TB control program in Ethiopia should increase its educational efforts among all TB suspects but particularly among jobless individuals to increase the uptake of HIV testing.

PC-100366-13   Fluoroquinolone use in an HIV treatment program in Western Kenya: implications for TB control

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Background: FQ have potent activity against TB and are the backbone of MDR regimens. Convenient dosing and broad spectrum of anti-bacterial activity make FQ popular for empiric treatment of respiratory tract and other infections. Prolonged/recurrent use of FQ by patients with undiagnosed TB leads to delay in diagnosis and risk for FQ-resistant TB. Understanding the current use of FQ in a large cohort of HIV-TB patients

is needed to inform local, national and global policies and recommendations for appropriate use of FQ.

Methods: USAID-AMPATH pharmacy database was used to identify patients at Moi Teaching and Referral Hospital receiving a FQ prescription (ciprofloxacin) between 5/06–9/08. Records for a randomly selected subset were retrospectively reviewed to confirm FQ prescription, clinical indication, length of therapy, patient demographic/clinical characteristics (age, sex, previous TB, CXR result, history of IPT, CD4, ARV regimen, date of TB diagnosis post FQ).

Results: Over 1900 FQ prescriptions dispensed. A randomly selected sample of 172 prescriptions (from 112 patients) was reviewed. FQ indications included cough/respiratory tract infection ($n = 51$, 30%), diarrhea/gastroenteritis ($n = 50$, 29%), urinary tract infection ($n = 25$, 14%), sexually transmitted infection ($n = 7$, 4%), fever ($n = 6$, 3%). 38 (34%) had a history of TB prior to FQ use. 11 (10%) were diagnosed with TB after FQ use (median CD4 285; 1 patient on ARVs, 1 had received IPT). Time from FQ to TB diagnosis: 5 patients received FQ in the 1 month prior to TB diagnosis, 2 between 1–3 months before TB diagnosis, 1 between 3–6 months before TB diagnosis, and 3 more than 6 months. 6 patients received more than one course of FQ prior to TB diagnosis. Median duration of FQ exposure was 15 days (IQ range 14–15).

Conclusion: FQ are widely used within AMPATH HIV care program for a variety of indications. Whether FQ use delays TB diagnosis or leads to TB resistance is of concern and requires further investigation.

PC-100538-13   Tuberculosis treatment related liver dysfunction in TB-HIV patients

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Setting: Tuberculosis (TB) patients with advanced age, jobless, low education with antecedent of allergy, alcohol abuse, low weight, low serum albumine, low TCD4 count and co-infected with HBV, HCV or HIV (+), are at high risk of drug induced liver injury (DILI) with anti TB drugs.

Objectives: To assess the incidence of drug induced liver in injury (DILI) and the clinical, paraclinical and risk factors of TB-HIV (+) patients under TB treatment.

Methods: Cross-sectional study with 151 TB patients including 78 TB-HIV (+) and 73 TB-HIV (−) at the provincial polyclinic of An Giang.

Results: Incidence of DILI among TB-HIV (+): 30.8% (24/78), sex ratio male/female 5:1 and incidence of DILI among TB-HIV (−): 21.9% (16/73), sex ratio: 2:1 ($P < 0.05$); Fever >380C (67%) and nausea-vomissement (67%) are the frequent signs of DILI in TB-HIV (+) patient ($P = 0.000$); 58.3% (14/24) of extrapulmonary TB-HIV (+) patients have

DILI ($P = 0.03$). In TB-HIV (+), abnormal liver function testing and DILI occurred after 2 weeks of TB treatment ($P < 0.05$). Age >35 y.o, jobless (in precarious economic condition), living near the boundary with Cambodia, low level of primary school education with antecedent of allergic history, alcohol abuse, low weight <35 kg, co-infected with HBV or/and HCV, low serum albumine ≤35 g/l and with severe immuno depression are the main risk factors for DILI in TB-HIV (+) patients when they are treated with anti TB drugs (OR > 1, $P < 0.05$)

Conclusion: Age, sex, jobless, allergic history, alcohol abuse, low weight <35 kg, co-infected with HBV or/and HCV, low serum albumine ≤35 g/l are the main risk factors for DILI in TB-HIV (+) patients under TB treatment at the provincial polyclinic of An Giang.

PC-100708-13   Tuberculosis in the context of widely available antiretroviral therapy: experience from a South African study

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Background: Even though antiretroviral therapy (ART) reduces the tuberculosis (TB) risk by 60 to 80%, HIV-associated TB continues to drive the TB epidemic in sub-Saharan African countries. We aim to describe the characteristics of hospitalized TB cases in an area with wide-spread and free access to ART.

Methods: Analysis of clinical and demographic data of TB patients discharged from the Johannesburg Helen Joseph Hospital TB Focal Point between October 2008 and December 2009.

Results: During the 15 month study period, 2802 TB patients were discharged via the TB focal point, of which 77% had been hospitalized. About half (53%) were female, median age was 37 years, and 14.7% had a history of TB treatment. Patients were diagnosed with pulmonary TB (PTB) only (45.1%), extrapulmonary TB (EPTB) only (39.4%) or PTB and EPTB (15.5%). Among the 2652 (94.6%) patients with known HIV status, 2318 (87.4%) were HIV-positive and 334 (12.6%) HIV-negative. Pulmonary involvement was less frequent among HIV-infected than HIV-negative patients (58% vs. 65.6%, $P = 0.01$). Among those HIV-positive, median CD4 count was 80 cells/mm³. Median CD4 count was lower among men compared to women (68 vs. 89 cells/mm³, $P < 0.001$), and among those hospitalized compared to outpatients (71 vs. 120 cells/mm³, $P < 0.001$). Mean CD4 count among patients with PTB only, EPTB only and PTB plus EPTB was 73, 99 and 62 cells/mm³, respectively. At time of TB diagnosis, 18% of HIV-infected patients were on ART. Median CD4 count

was higher among those on ART compared to those not on ART (95 vs. 76 cells/mm^3, $P = 0.003$). Prior to discharge, patients with CD4 below 200 cells/mm^3 were referred for ART and 87.5% were on cotrimoxazole prophylactic treatment.

Conclusion: The majority of patients hospitalized with TB at an inner city hospital in a region with widespread and free ART failed to access ART prior to developing TB, had severe immune suppression (median CD4 count 80 cells/mm^3), and were diagnosed with EPTB (54.9%).

PC-100978-13   Assessment of some immunological and haematological parameters in pulmonary tuberculosis patients

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Background: Nigeria has an estimated TB-HIV co-infection rate of 27% and additional 50 000 annual TB cases from pool of people living with HIV/AIDS. TB clinics are the first point of contact because TB is often the disease that initially causes HIV-positive people (unaware of their HIV status) to seek care. Risk of developing HIV/AIDS increases when TB infection co-exists with HIV, causing deficiencies in the immune system.

Design and methods: The study was based on the assessment of some immunological/haematological indices in subjects with pulmonary tuberculosis (PTB) patients attending central Hospital, Benin City. 211 TB suspects (114 males and 97 females) were enrolled. The prevalence of TB, CD4/CD8 ratio of infected individuals, haematological parameters profile, and the coexistence rate of TB with other infections such as TB and hepatitis B surface antigens were determined. Analyses included use of χ^2, analysis of variance (ANOVA) test and student's t-test.

Results: The study revealed PTB prevalence of 17.5% and 12.5% in both sexes. Subjects above 50 years recorded higher prevalence in both sexes. Decrease in transmission results to a shift in caseload of older age groups with higher proportion of cases coming from the reactivation of latent infection. There is marked decrease in CD4 and CD8 counts of TB-HIV co-infected patients with increased monocytes. PTB prevalence is high among males and females above 50 years; ($P < 0.05$). 32 subjects diagnosed with TB, 20 males and 12 females. 3 (15.0%) male and 3 (25.0%) had PTB and HIV. Mean CD4 and CD8 of PTB co-infected males and females revealed a significantly low CD4 and CD8 cells count ($P < 0.05$).

Conclusions and recommendations: 1) Advocate best practices in diagnosis of TB in HIV infected individuals using quality laboratory systems; 2) strengthen collaborative efforts of HIV and TB programs at all levels; 3) upgrade facility to bio-containment level to enhance laboratory diagnosis.

PC-101113-13   Mortality risk factors in patients with hepatitis C and HIV-associated tuberculosis

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Introduction: Infection with hepatitis C virus (HCV) and human-immunodeficiency-virus (HIV) is one of the most challenging co-morbidities emerging in tuberculosis-infected patients. Medications for treatment of TB, HIV and HCV are hepatotoxic.

Objectives: To determine mortality risk factors and TB treatment outcome among patients infected with TB, HIV and HCV.

Table   Characteristics of patients with TB-HCV-HIV co-infection

Patient characteristics	Patients without in hospital mortality ($n = 57$)	In hospital mortality ($n = 10$)	P value
Age in years			0.14¶
Median	37	35	
Range	16–79	17–58	
Marital status, n			0.047‡
Single	33	70	
Married	40	30	
Divorced	27	0	
Median hospitalization length, days	28	24	0.55¶
Jobless, %	43	50	0.55‡
Smoker, %	100	100	
Opium addict, %	89	90	
IVDU, %	89	70	0.17‡
History of incarceration, %	87	70	0.11‡
Symptoms, %			
Cough	74	80	
Hemoptysis	5	0	
Chest pain	30	10	
Dyspnea	63	40	
Weight loss	74	60	
Loss of appetite	60	40	0.30‡
Toxoplasmosis	11	30	0.09
Oral candidiasis	19	20	
Laboratory data			
WBC (Mean)	5971	4366	0.08¶
Hgb	11.2	9.8	0.050¶
Plt	204 964	112 900	0.0000¶
Elevated ALT, %	23	60	0.02‡
Elevated AST%	63	90	0.14‡
CD4, %			0.087‡
<200	79	60	
200–500	9	0	
>500	12	40	

Methods: In a retrospective study medical records of all admitted TB-HIV-HCV co-infected patients in the National Research Institute of Tuberculosis and Lung Disease (NRITLD) were reviewed. A standardized data sheet was applied to collect demographic, clinical, laboratory and microbiologic data. Presenting signs and symptoms, co-morbidities and widespread lab data (including biochemical, hematological and serologic assay) were measured.

Results: Analysis of 67 TB-HIV-HCV co-infected patients showed all of them were smoker males, 44.78% jobless, 38.81% single, 22.39% divorced, 86.57% IVDU, 89.55% opium user, 10.45% HBsAg+, 85.07% imprison ship and 14.93% were died in hospital. Among different demographic factors, there was an only significant difference in marital status. No significant clinical symptom was discriminative. Statistical analysis of laboratory data showed that platelet level, Hgb and WBC were significantly low in patients with in hospital mortality. Elevated liver enzyme was more common among patients with in hospital mortality.

Conclusion: These findings imply that physician should pay more attention to liver function tests and complete blood count in these patients. This study like previous studies clarifies that the rate of anti-tuberculosis therapy induced hepatoxicity in HCV-HIV co-infected patients is similar to other patients; but the specific situation of TB-HIV-HCV infected patients needs more attention to LFT.

PC-101207-13   Isoniazid preventive therapy implementation, adherence and determinants in Dire Dawa, Ethiopia

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Aim: Scientific information on the number of isoniazid preventive therapy (IPT) beneficiaries, their rate of adherence vis-à-vis determinants of adherence is scarce in Ethiopia. This study assessed patient characteristics, patient care indicators and organizational factors in relation to IPT service implementation and adherence to treatment.

Methods: The study was conducted in five public health facilities of Dire Dawa city administration. Data on self-reported adherence was collected from 238 PLHIV who were on IPT by the time of visit through patient exit interview. Organizational and service related data were collected through in-depth interview and structured observation.

Results: The health facilities were organized in such a way that enabled them to provide comprehensive HIV care services. With some observed differences among facilities, service integration, staffing, patient-provider relationship, laboratory services and drugs supply were found to be well organized. However, there was low IPT service coverage with only 179 (32.8%) individuals receiving isoniazid (INH) among the eligible 480 cases. With 94.8% response rate, the self-reported full adherence rate was 78.5%. The most frequently forwarded reasons for missing INH doses were being away from home, forgetfulness and running out of pills. There was no significant association between socio-demographic variables and level of adherence.

Conclusion: IPT service implementation is weak in Dire Dawa, both in terms of reaching those who needed the service and in attaining appropriate adherence level. It was also found that increasing IPT coverage and improving adherence require much more than quality guidelines and adequate organizational capacity. Health care providers' attitude and follow-up are found to be the main challenges for better service utilization and adequate adherence.

ADULT LUNG HEALTH

PC-101422-13   Biomass flame and lung health: an awareness campaign

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Hundreds of millions of people across the globe (mostly in developing countries) are suffering from various lung problems arising out of use of biomass fuels like wood, charcoal, agricultural residue and animal dung (traditional fuel). As per IEA 2002, 1/3 of the world population, about 2.4 billion burn organic matter primarily for cooking, heating and lighting leading to an increase in indoor air pollution. Most of them live in rural areas, have low income and lack access to modern fuel. There is an increased incidence of acute respiratory infections including pneumonia, TB, COPD, asthma and lung cancer. Indoor air pollution (IAP) is associated with impaired lung function due to pollutants like carbon monoxide and particulate matter. As per WHO, more than 1.5 million deaths occur each year mostly in developing countries and above 38.5 million disability adjusted life years can be attributed to indoor smoke emerging from solid fuels. Women and children are more prone as they are confined indoor. In the wake of International Year of the Lung, 2010, this paper attempts to study the impact of biomass fuels on lung health of people at global level. Moving from macro to micro level of creating awareness amongst people at the individual and higher level (centre and state) requires intensive communication, resource mobilization, management and sensitization of people to create in them a strong conviction to move from biomass fuel to safer and health friendly methods of cooking

and heating. Though measures are being taken at larger level to bring this transition, this paper highlights how Each One–Teach One method can prove to be more effective in creating awareness amongst the not so highly literate and educated part of the population. Use of management skills to enhance their perception and awareness for health promotion (from individual to family to society to nation and the globe) is the highlight of this paper.

PC-100821-13 Prevalence of asthma symptoms in adult university students and workers in Dongola, North Sudan

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Introduction: Asthma is a chronic inflammatory disorder of the airways characterized by reversible airflow obstruction. Morbidity and mortality rates of asthma have been increasing all over the world. In Sudan the prevalence of asthma symptoms in adult Sudanese university students and workers has been investigated in Khartoum state (capital of Sudan) and it was found to be 9%.
Objectives: 1) To estimate the percentage of asthmatics among Sudanese university students and adults living in Dongola; 2) To validate the adapted ISAAC questionnaire by pulmonary function tests in subjects with asthma symptoms; 3) To identify the common triggering factors for asthma symptoms in the affected group.
Method: Cross-sectional study performed in Dongola town about 480 Km northern Khartoum during December 2009. A modified ISAAC questionnaire was distributed using stratified random sampling. Any subject with asthma symptoms was interviewed by another questionnaire specially designed for asthma subjects covering asthma symptoms, allergy symptoms and environmental factors. In addition, lung function tests and skin prick tests had been done to all those claiming to have symptoms of asthma.
Results: 394 subjects were included. Prevalence of asthma according to wheeze alone was 10.7%. Prevalence of asthma depending on wheeze plus shortness of breathing was 8.1%. Most of the patients have intermittent symptoms. Reversibility test was positive in 32.5% of asthmatic group. Trigger factors include house dust (76%), trees (23.8%) and animals (11.9%).
Conclusion: 1) Prevalence of asthma depending on wheeze plus shortness of breathing among Sudanese adult university students and workers living in Dongola town is 8.1%; 2) The use of combination of asthma symptoms such as wheeze plus shortness of breathing or nocturnal cough was found to be better to estimate the prevalence of asthma in Sudan;

3) House dust is the most important triggering factor among asthmatic group (76%).

PC-100709-13 Les manifestations allergiques chez les enfants de 13–14 ans en milieu scolaire à Lomé, Togo

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Cadre : Les manifestations allergiques prennent de plus en plus une place importante en pratique médicale et commencent à poser des problèmes de santé publique dans les pays en developpement.
Objectif : Le but de l'étude étaiet de déterminer la prévalence des maladies allergiques chez les enfants en milieu scolaire à Lomé.
Méthode d'étude : Il s'agissait d'une étude prospective transversale réalisée de novembre 2001 à janvier 2002 dans 23 collèges d'enseignement général de Lomé. Tous les élèves de 13–14 ans consentant à participer à l'étude avaient rempli la version française de l'auto questionnaire.
Résultats : 2782 élèves de 13–14 ans, 56% de garçons et 44% de filles, avient participé à l'étude. 16,6% ont signalé des symptômes d'asthme, avec sévérité chez 1,6%. 10% avaient un antécédent d'asthme. Les signes de rhino conjonctivite étaient retrouvés chez 23,1% et l'eczéma chez 15%. Les associations asthme-rhino conjonctivite, asthme eczéma et rhino conjonctivite eczéma étaient retrouvées respectivement chez 7%, 4,5%, et 5,8% des élèves. Une proportion de 2,44% des élèves signalé les signes des trois manifestations.
Conclusion : Les manifestations allergiques sont des réalités non négligeables chez les enfants au Togo.

PC-101145-13 Validation of the ACT questionnaire and GINA 2006 in the classification of asthma by level of control

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Context: In clinical practice, the GINA recommend the classification of asthma by level of control but its implementation is complicated by the need of the functional respiratory exploration which cannot be available in most of the health posts. The Asthma Control Test questionnaire was developed to help medical doctors to classify with accuracy asthma by level of control without the use of functional respiratory exploration. It is a simple, cheap, accurate and efficient tool to assess this level of control. It has been validated in many different countries but not yet in Viet Nam.
Objectives: To validate the ACT questionnaire and to compare with the criteria from GINA 2006 in the classification of asthma by level of control.

Methods: This is a cross sectional study with 124 asthmatic patients diagnosed and treated at the Medical and Pharmacy University Hospital of HCMC from Feb 2006 to Feb 2007.

Results: From the study, the results show that the percentage of the complete control of asthma level according to the criteria from GINA 2006 is higher compare with those from the ACT questionnaire ($P = 0.032$) while the percentage of the partially complete control with the ACT is higher than with those of GINA ($P = 0.033$). The percentage of the level of no control of asthma was similar in the 2 groups ($P = 0.34$). However, there is no statistical difference ($P = 0.08$) in the group of control and complete control in the classification from GINA 2006 (88/124 = 70.97%) and from ACT (85/124 = 68.55%).

Conclusion: The classification of asthma by level of control with ACT questionnaire is comparable with the classification from GINA 2006. With the ACT questionnaire, the asthmatic patients can assess their disease at home since it is a simple, cheap, accurate tool for monitoring the disease without the need of functional respiratory exploration and enhances the collaboration between the doctor and the patient and increasing its adherence to treatment.

PC-100215-13   Effect of bilevel non-invasive positive airway pressure ventilation

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Objective: To evaluate the effect of Bilevel non-invasive positive airway pressure ventilation (BiPAP) in the treatment of acute respiratory failure (ARF).

Method: The clinical experimental study.

Results: From 06/2008 to 06/2009, 79 patients with ARF (41 hypercapnic and 38 hypoxemic) were treated by non-invasive ventilation (40 BiPAP and 39 CPAP). The incidence ratio in male and female was 1.55:1. The average age was 64.4 ± 14.67 (range, 22–90 years old). All of them showed signs and symptoms of serious ARF, such as decreased perception, rapid breath, tachycardia, high blood pressure, APACHE at 20.4 ± 4.82 (with estimated death rate at 35%), low pH, high $PaCO_2$ and ratio of $PaO_2/FiO_2 < 200$. 79.75% cases had combined at least two underlying diseases. Most of the patient's features between BiPAP group and CPAP group were not different significantly. BiPAP group was set up parameters of ventilation: IPAP: 18.7 ± 2.52 cmH2O; EPAP: 6.4 ± 1.93 cmH2O; and FiO2: 51.8 ± 11. After 2 hours with non-invasive ventilation, 70.9% cases had improved clinical symptoms and arterial blood gas ($P < 0.05$). Arterial blood gas was improved better in BiPAP than in CPAP ($P < 0.05$). The effect of BiPAP was 1.69 times than of CPAP in patients with hyper-

capnic ARF (RR = 1.69; 95%CI: 0.98–2.91; $P = 0.041$). Simultaneously, the failure rate in BiPAP group was lower than in CPAP group (20% versus 38.5%), with common failure causes such as ineffective ventilation after 2 hours (14/23 cases) and patients' uncooperativeness with treatment (5/23). However, there were not different from failure causes among two groups. Besides, BiPAP had caused little skin redness with face mask (22.5%), light flatulence (12.5%) and no serious complications.

Conclusion: After two hours treating ARF, BiPAP improved clinical symptoms and arterial blood gas with high success, safety, and helps to avoid serious complications caused by mechanical ventilation with tracheal intubation.

PC-100382-13   Assessing community-acquired pneumonia severity in Malawi: CRB-65 and derivation of a severity index

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Background: The CRB-65 score (confusion, resp. rate > 30, BP < 90/60, age > 65) is an effective tool for assessing severity of community acquired pneumonia (CAP). We assessed its validity in a Malawian hospital population and identified variables predictive of mortality to derive an accurate severity score for this setting.

Method: Data for 43 variables, recorded in the first 48 hours of admission, was collated for all patients admitted to Queen Elizabeth Central Hospital (QECH), Blantyre for management of CAP, over 2 months ($N = 216$). The efficacy of CRB-65 in predicting mortality was investigated. A multivariate analysis identified predictor variables, to create a new severity score.

Results: Median age was 37, HIV prevalence 77.8% and overall mortality 18.4%. CRB-65 showed low sensitivity and specificity in predicting mortality, indicated by the area under the ROC curve (AUC): 0.648. Mortality for scores 0–3 was 6%, 20%, 26% and 33%. No patients scored 4. Independent predictors in a multivariate analysis; male sex, 'S' (AOR 3.2, $P = 0.04$); wasting, 'W' (AOR 4.6, $P = 0.002$); requiring assistance to walk, 'A' (AOR 4.6, $P = 0.0001$); temp >38°C or <35°C, 'T' (AOR 10.8, $P = 0.003$); BP < 100/60, 'Bp' (AOR 4.6, $P = 0.01$). A severity index using these factors (SWAT-Bp) has high sensitivity and specificity in predicting mortality (AUC 0.911). Mortality for scores 0–5 was 0%, 2%, 7%, 36%, 77% and 100%. A score >2 was 84% sensitive and 87% specific for mortality prediction.

Table Efficacy of SWAT-Bp scoring in predicting mortality from CAP

Test characteristics for in-hospital mortality

SWAT-Bp score	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
⩾0	100	—	17.2	—
⩾1	100	17.4	20.0	100
⩾2	96.8	52.3	29.7	98.7
⩾3	**83.9**	**86.6**	56.5	96.3
⩾4	54.8	97.3	81.0	91.2
5	12.9	100	100	84.7

Conclusion: We identified variables predictive of CAP severity in QECH, Blantyre. CRB-65 lacks efficacy in severity assessment of this population. A score combining 'male sex', 'wasting', 'requiring assistance to walk', 'high or low temperature' and 'hypotension' can accurately stratify patients; ⩽2 indicates non-severe pneumonia (mortality 3.7%) and ⩾3 severe illness (mortality 56.5%). This tool requires validation in other populations to determine its utility in guiding management of CAP in resource-poor settings.

PC-100044-13 Pattern of presentation of lung cancer in Sudan

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Lung cancer is the commonest type of cancer in the western world. Early detection offers the best chance for cure. Generally lung cancer is believed to be rare in Africa where infections especially tuberculosis dominate the spectrum of clinical pulmonary medicine. Because of this it is possible that some cases of lung cancer are missed or diagnosis is delayed. Description of pattern of presentation of lung cancer in our community would alert physicians to the presence of this condition and help in making early diagnosis. For this purpose ninety-four consecutive patients with histological proven lung cancer were studied. Sixty were male (62%). The main age was 58 years; fifty-eight patients (61%) were current or previous smokers. The most common presenting symptom was cough which occurred in 83 patients (88%), followed by shortness of breath in 67 patients (71%), and chest pain in 52 patients (55%). The commonest physical sign was pleural effusion that occurred in 37 patients (39%), followed by consolidation in 23 patients (24%) and collapse in 20 patients. The common radiological finding was lung opacity that occurred in 56 patients, followed by collapse and pulmonary nodule in 20 patients (22%) each. Eighty-three patients (88%) had non-small cell lung cancer, of these 83 patients only 11 patients (13%) were potentially operable (stage 1 or 2). Symptoms, signs, and radiology of lung cancer mimic other pulmonary conditions. Lung cancer should always be considered as differential diagnosis and investigated promptly; the most remarkable finding in this study is the high percentage of advanced disease at time of diagnosis. Delayed diagnosis a possible cause.

PC-100591-13 Factors of long and short term survival in advanced non small cell lung cancer: a prospective study

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Non small cell lung cancer (NSCLC) prognosis, especially in advanced stages, is poor. Clinical experience showed that disease evolution is heterogeneous. A small number of patients, called long term survivors (LS) survive more than 18 months. Others survive less than 6 months, they are called short term survivors (SS). Our study aims to focus on clinical radiological and biological aspects in LS compared to SS. A prospective case control study was carried out including 2 groups, diagnosed between January 2007 and June 2009: 17 LS and 22 SS. All patients had advanced lung cancer IIIA, IIIB, IV. LS were 58.8 years-old mean aged men vs. 63.7 years-old mean aged men in SS. All LS were smokers vs. 87% in SS. Haemoptysis at presentation was more frequent in SS (60%) than in LS (23.52%). Weight loss was more frequent in SS (86.66% vs. LS 64.7%). Body mass index (BMI) <18.5 was found in 11.76% of LS vs. 26.66% in SS ($P < 0.05$). However, performance status (PS) 2 was found only in LS (17.64%). 53.33% of SS had PS = 1 vs. 23.52%. 35.3% of LS had stage IV vs. 53.33% in SS. Adenocarcinoma was more frequent in LS (35.3% vs. 20%). Epidermoid carcinoma was the predominant histological type in both SS and LS (46.66% vs. 41.17%). Cerebral metastasis was especially found in SS 26.66% vs. 11.76% ($P < 0.05$). Analysis of haematological disorders revealed a significant difference between the 2 groups in anaemia (23.53% in LS vs. 80% in SS; $P = ?$). CRP increase and a hypocalcaemia were mostly recorded in SS compared to LS. Chemotherapy was achieved in 64% of LS vs. 66.66% in SS. All patients received bitherapy including platinum. The mean survival was 19.12 months in LS vs. 2.29 months in SS. In LS survival ranged between 12.53 months and 33.13 months vs. 0.37 months and 5.7 months in SS. Analysis of characteristics of the two groups is interesting to identify factors associated with longer survival influencing prognosis and therapeutic decisions.

TB DIAGNOSTICS I

PC-100495-13   Poor correlation of smear microscopy for TB culture on solid and in liquid media during TB treatment

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Background: Sputum culture is considered the gold standard for diagnosing TB and monitoring treatment but it is often unavailable in resource-poor settings. Therefore, many national TB programmes base management decisions on smear microscopy performed during treatment.
Objective: This study investigates the relationship between smear microscopy and culture during TB treatment.
Methods: We analysed mycobacteriological results of serial sputum samples, submitted weekly for 8 weeks and monthly thereafter, during the first 17 weeks of TB treatment from 447 patients enrolled in the treatment-shortening REMox study. Patients were adults with smear-positive pulmonary TB, HIV-negative or HIV-positive with CD4 > 250 cells/μL, and received standard TB treatment or a 4 month regimen in which moxifloxacin replaced either isoniazid or ethambutol. Samples were processed for smear microscopy by Ziehl-Neelsen staining and for culture in both solid Löwenstein-Jensen (LJ) and liquid MGIT (mycobacterial-growth-in-tube) media. Predicted probabilities and odds ratios were calculated using mixed effects logistic regression.
Results: 6496 samples were analysed. Paired smear and LJ-culture data were available for 4422 samples. 4681 samples had paired smear and MGIT-culture results. The probability of a positive culture at week 8 given a positive smear was 0.75 on MGIT and 0.12 on LJ. The odds ratio reflecting the association between the culture result and the smear result was high but had very wide confidence intervals and decreased with time (Table). Similar relationships were observed for quantitative smear results. These results did not differ by HIV status.
Conclusion: Smear microscopy is a poor predictor of solid and liquid culture results during TB treatment, and the strength of the association decreases with time over the course of treatment. This may have implications for national programmes advising treatment decisions based on smear microscopy.

Table   The predictive probability (PP) with 95% confidence interval of a positive culture on LJ or MGIT at weeks 0 to 17 visits given the smear result at that visit

Visit Week	Smear negative PP	95%CI	Smear positive PP	95% CI	Odds ratio (95%CI)
LJ					
4	0.24	(0.15–0.38)	0.85	(0.76–0.90)	10.1 (4.9–20.7)
8	0.01	(0.01–0.04)	0.12	(0.06–0.23)	7.2 (3.9–13.2)
12	0.00	(0.00–0.01)	0.05	(0.02–0.13)	4.0 (1.9–8.4)
17	0.01	(0.00–0.03)	0.08	(0.02–0.30)	2.9 (1.1–7.8)
MGIT					
4	0.69	(0.59–0.77)	0.96	(0.92–0.98)	17.1 (7.6–38.7)
8	0.30	(0.23–0.37)	0.75	(0.64–0.84)	9.2 (2.9–29.6)
12	0.10	(0.07–0.14)	0.30	(0.19–0.45)	38.3 (3.9–370.7)
17	0.09	(0.06–0.13)	0.21	(0.10–0.40)	8.5 (1.4–50.9)

PC-100042-13   Operational effectiveness of TB culture and drug susceptibility testing in a high-prevalence setting

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Background: Liquid culture systems are available for TB testing that provide higher sensitivity than Ziehl-Neelson (ZN) microscopy and allow rapid concurrent testing for drug-resistance. Their scale-up is recommended in low- and middle-income countries but data on their effectiveness under operational conditions is scant.
Setting: Shantytown with 500 000-person population in Northern Lima, Peru that principally utilized ZN microscopy for TB diagnosis from 2002–2010.
Methods: The high number of TB suspects (>100 daily) did not allow culture testing of every sample therefore culture was focused on two high-risk groups: TB patients and their symptomatic contacts. 4267 Microscopic-Observation Drug-Susceptibility (MODS) cultures were performed for TB detection and concurrent drug-resistance testing.

Results: MODS testing of 2932 TB patients determined that 381 (13%) had drug-resistant TB (DRTB; i.e. resistant to isoniazid, rifampicin or both), so 7.7 patients needed to have MODS culture per drug-resistant case identified (16 per MDR case). Drug resistance was more common among re-treatment cases (26%; risk ratio = 1.9, $P < 0.001$; population attributable fraction: 16%). Thus, restricting MODS testing to the 22% of TB patients who were re-treatment cases would only detect 35% of all DRTB (39% of MDR-TB). Additionally among 12 581 contacts, 1335 (11%) had respiratory symptoms, 113 of whom were MODS culture positive (i.e., 0.9% of all contacts and 8.5% of symptomatic contacts). Of these culture-positive contacts 39 (35%) were ZN microscopy-negative. Thus 34 symptomatic household contacts needed to have MODS culture per smear-negative TB case identified.

Conclusion: In operational settings, modern diagnostic tests that offer sensitive diagnosis and rapid DRTB testing may provide greatest public health impact when focused on TB patients rather than on enhanced case-finding. These calculations may be adjusted for settings with different rates of smear-negative TB and DRTB.

PC-101296-13   A simple colour test for diagnosing MDR-TB and XDR-TB under field conditions

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Background: Increasing rates of drug-resistant and smear-negative TB require improved TB diagnostics that are easy to use, affordable and equipment-minimal. The MDR/XDR-TB Colour Test is a simple, Thin-Layer-Agar-based non-proprietary culture technique that offers concurrent MDR testing and XDR screening. We compared its performance with a standard culture technique.

Methods: Sputum samples were collected from patients with suspected TB ($n = 788$). Smear microscopy was done directly from sputum samples, which subsequently underwent culture with the Peruvian standard protocol of modified-Petroff NaOH-decontamination and culture on Ogawa medium. Samples for the Colour Test were collected in parallel directly into sputum pots containing disinfectant that decontaminated the sputum in-transit. Upon arrival in the lab, these were directly applied to selective culture medium without any processing. Positive cultures were indicated by colour change.

Results: 265 samples had a culture-positive result and
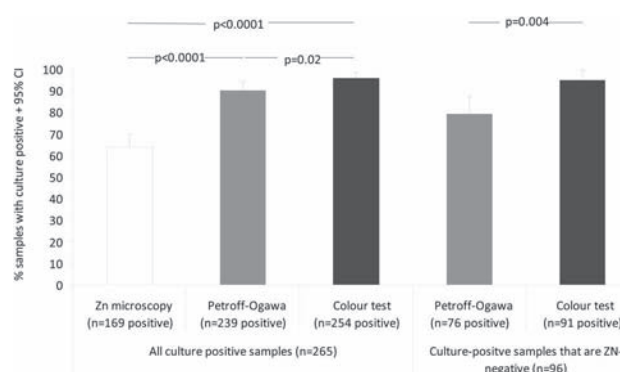
both Colour Test and Petroff-Ogawa were significantly more sensitive than ZN microscopy (96% and 90% vs. 63%; $P < 0.0001$). The Colour Test also had higher sensitivity than Petroff-Ogawa ($P = 0.02$) and this difference was greatest in the 128 smear-negative samples that were culture-positive (95% vs. 79%; $P = 0.002$). Results were obtained more rapidly in the Colour Test (17 vs. 21 days; $P < 0.0001$) with similar contamination rates (3.5% vs. 2.4%; $P = 0.2$). The Colour Test detected drug-resistant TB in 18% of all culture-positive samples the same day as culture detection with 99% agreement with delayed indirect testing.

Conclusion: The Colour Test is a simple culture technique that offers superior characteristics over the current standard culture method. It addresses the rising challenges of paucibacillary disease and drug-resistance while using simple and effective technology that is appropriate to resource-poor settings where these problems are most common.

PC-100618-13   Rapid direct MDR-TB testing better predicts clinical outcome than conventional delayed testing

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Background: Drug susceptibility testing (DST) is an important tool in the control of multidrug-resistant tuberculosis (MDR-TB). Conventional DST is done indirectly after first culturing the TB strain, thereby delaying the DST result. New DST tests are emerging that culture TB directly on antibiotic-containing media concurrently with drug-free culture. This leads to a much more rapid DST result, which may have an important positive impact on the patient's clinical outcome. Direct and indirect DST may have discrepant results and we therefore investigated the clinical

outcome of patients in relation to the agreement of results of both methods.

Methods: Direct and indirect DST was performed on the same sputum sample ($n = 2081$) and the data were then grouped according to the concordance of the results (both MDR, both not MDR or discrepant result). For each pair of results we obtained the data on the patients' clinical condition at the end of TB treatment and the cured patients were followed-up for the emergence of a new episode of TB. We compared the risk of having a bad clinical outcome (failure, death or recurrent TB) for each group.

Results: Direct and indirect DST had consistent results in 97% of samples. Patients with an MDR result in direct DST and a non-MDR result in indirect DST had a hazard ratio of 7.3 (95%CI 4.2–12.8) of having a bad clinical outcome compared to the patients with no evidence of MDR-TB. Patients found to be MDR in both methods had a hazard ratio of 2.9 (CI 95% 2.6–3.5) of having a bad clinical outcome compared to the patients with no evidence of MDR-TB.

Conclusion: Patients diagnosed with MDR-TB by direct DST but diagnosed to have non-MDR-TB by indirect DST had the highest risk of having a bad clinical outcome. Thus, these results of rapid direct DST had greater clinical significance than slower indirect DST.
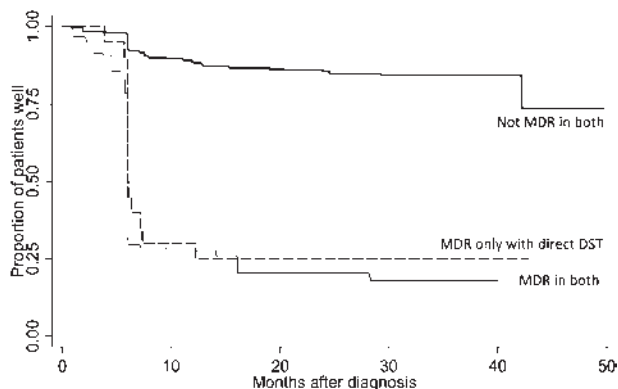
PC-101139-13   Pyrazinamide susceptibility testing: comparison of MGIT assay with Wayne test and gene sequencing

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Aim: For the management of multidrug-resistant (MDR) tuberculosis, pyrazinamide (PZA) susceptibility testing of *Mycobacterium tuberculosis* is required for designing optimal regimen for treatment. To select an accurate and simple test, we accessed performances of a commercial BACTEC™ MGIT™ 960 PZA (MGIT) assay (Becton Dickinson, Sparks, MD, USA), the Wayne test and the pncA gene sequencing.

Methods: The commercial MGIT test was a liquid culture based method, the Wayne test was an enzymatic pyrazinamidase assay and mutation of the pncA gene sequencing were used to detect PZA resistance. A total of 196 MDR *M. tuberculosis* isolates were evaluated using three methods in parallel.

Results: Using the pncA gene sequencing as a gold standard method, our results indicated that the sensitivity, specificity and accuracy for the MGIT assay were 77.1%, 97.1% and 72.5%; while for the Wayne test were 96.8%, 100% and 98.5%, respectively. The turn-around-time (TAT) was 10 days for the MGIT assay, 7 for the Wayne test, and 3 for the pncA gene sequencing. In addition, for each isolate, the cost of the MGIT assay was 19 USD, the Wayne test 0.4, and the pncA gene sequencing 20.

Conclusion: The Wayne test showed better concordance with sequencing results in comparison with the MGIT assay. The Wayne test was recommended to be included in routine clinical services with the pncA gene sequencing as a supplement.

PC-101136-13   Influence of race/ethnicity in quantitative interferon-γ response

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Background: Interferon-γ release assays (IGRAs) have been recommended by national and international agencies for targeted screening of LTBI, though differences in elicited quantitative responses according to race/ethnicity have not been evaluated.

Design/methods: Clinical and laboratory data from patients referred to the San Francisco Department of Public Health Tuberculosis Control Clinic from March 2005 to February 2008 were reviewed. We excluded subjects with active or clinically inactive disease, HIV-infection, immunosuppressive conditions, or who were under 15 years of age. We used negative binomial regression with robust standard errors to model racial/ethnic differences in IFN-γ results obtained from Quantiferon TB-Gold, adjusting for age, gender, ATS/CDC/IDSA TB Classification, length of time in the United States, contact status, recent skin test placement, and homelessness.

Results: Of 1375 eligible subjects, 694 (50%) were Asian, 251 (18%) were White, 160 (12%) were Black, and 270 (20%) were Hispanic. Median IFN-γ levels varied significantly by race/ethnicity (Asian, 0.5 IU/ml (IQR 0.04–1.59); White, 0.11 IU/ml (IQR 0.01–0.87); Black, 0.57 IU/ml (IQR 0.01–4.54); Hispanic, 0.69 IU/ml (IQR 0.04–2.61); $P < 0.0001$). Among subjects with latent TB infection, Hispanics had higher adjusted mean IFN-γ levels compared to Asians (dif-

ference 0.768 IU/ml (95%CI 0.21 1.30; $P = 0.007$)) or Whites (difference 1.245 IU/ml (95%CI 0.597 1.89; $P < 0.001$); Blacks also had higher adjusted mean IFN-γ levels compared to Asians (difference 1.413 IU/ml (95%CI 0.503 2.323; $P = 0.002$)) or Whites (difference 1.901 IU/ml (95%CI 1.10 2.70; $P < 0.001$)).

Conclusion: In a TB referral center serving an ethnically diverse population, higher quantitative IFN-γ results were noted among Black and Hispanic patients with latent TB infection as compared with Asian and White patients. The cause and clinical significance of these differences should be considered in future studies.

PC-101288-13   Sputum smear quality as assessed during random blinded rechecking in a South Indian state

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Background: Under India's Revised National Tuberculosis Control Programme (RNTCP) in a south Indian state (Andhra Pradesh), ~120 000 sputum smears are examined every month in 918 designated microscopy centers (DMCs) by Ziehl-Neelsen staining for the presence of acid fast bacillus (AFB). As part of random blinded rechecking (RBRC) procedure (a component of quality assurance protocol) the laboratory supervisors assess the quality of ~10 000 randomly selected smears from all DMCs every month. The quality of smears is assessed by its size, its thickness, its evenness, staining and whether 10 white blood cells per high power field (WBC/hpf) are seen or not.

Objectives: We studied the quality of sputum smears as assessed by the laboratory supervisors during RBRC.

Methods: We used a retrospective cross sectional study design and reviewed RBRC records of a randomly selected month (Oct 2008). A sputum smear was defined as 'optimal' if the size is 2 cm by 3 cm, evenly spread, neither too thick or too thin, staining is neither under-decolorized nor over colorized and when seen microscopically >10 WBCs/hpf are seen.

Results: The records were available for 822 (89%) MCs from whom a total 9345 slides were rechecked. This included 91% of the smears that were negative for AFB and 9% of the smears were positive for AFB. The smear size was 2 cm by 3 cm in 6816 (73%) smears, the thickness of 6402 (68.5%) smears was good, and 6037 (65%) smears were 'even', the stain-

ing was good in 7163 (77%) smears and in 5635 (60.3%) smears >10 WBCs/hpf were seen. Overall 3239 (35%) smears were 'optimal'.

Conclusions: Sub-optimal quality may affect the detection of errors in the smear results during RBRC. Further studies may assess the factors contributing to sub-optimal quality and identify the interventions needed to improve the quality of sputum smears.

PC-101338-13   Does task shifting in TB microscopy to non-certified microscopists affect quality?

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Setting: Afghanistan has suffered the disruption of years of war which has had dramatic effects on all social structures, including TB services; 40% of the TB microscopy centers in the country are staffed with non-certified, trained microscopists. This action has been necessary in order to provide services to patients who would otherwise not have any access. However, the quality of work undertaken by non-certified, trained microscopists has never been critically evaluated.

Objective: The objective of this cross-sectional study was to assess the quality of smear microscopy slides collected for quality assurance under the National TB Control Program, and to compare the quality of sputum smear examinations between microscopists who are fully certified as laboratory technicians with those who do not have such certification.

Design: In this cross-sectional study, during a targeted period from July to September 2009, 7313 slides from 386 microscopy units in 30 provinces of Afghanistan were collected and cross-checked as part of a routine external quality assurance program. Information on certification status was obtained from the Human Resource Database of the Ministry of Public Health.

Result: The quality of work of certified laboratory technicians was not significantly different from those who did not have such certification when judged in terms of the number of slides in which a major error would have led to a false diagnosis (OR 1.11; 95%CI 0.64–1.94).

Conclusion: The results of this study justify the ongoing use of non certified microscopists in tuberculosis microscopy services in rural Afghanistan.

PC-100139-13   Adherence to national guidelines in the diagnosis of sputum-negative tuberculosis

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Background and challenges to implementation: The HIV epidemic has increased the occurrence of smear-negative pulmonary tuberculosis. This poses a serious challenge, since HIV changes the clinical presentation of TB, making diagnosis more difficult. It is estimated that in Uganda around 50% of all TB patients are HIV co-infected. In Gulu district, located in northern Uganda where HIV prevalence of 8.2% is higher than the national average, TB accounts for 30% mortality in patients with sputum negative TB. This study assessed adherence to national standardized guidelines for diagnosis of sputum negative TB.

Intervention or response: A retrospective analysis of patient records from hospital TB registers and in-patient case notes was conducted to verify whether clinicians followed the recommended diagnostic algorithm. The algorithm include i) a two-week history of cough, ii) no response to a course of broad spectrum antibiotics, iii) two negative sputum smears for acid-fast bacilli, and iv) a chest radiograph with abnormalities consistent with TB.

Results and lessons learnt: From a cohort of 370 patients diagnosed and treated for tuberculosis in 2008 in Gulu regional referral hospital, 154 patients (42%) were found to be smear-negative. All 154 patients had chronic cough ($\geq$2 weeks), 147 patients (96%) had received a two week broad spectrum antibiotic, 39 (25%) had at least two sputum smears done and 117 (76%) had a chest radiograph done. Only 22 out of 154 patients (14%) had all the four diagnostic criteria met. Additionally, 29 (32%) of the 92 patients who tested for HIV were found HIV-positive.

Conclusions and key recommendations: The standardized sputum-negative TB diagnostic algorithm was sub-optimally used with over reliance on chest radiography. These guidelines remain crucial in resource limited settings and refresher training, mentoring and supportive supervision of health workers is necessary to minimize over diagnosis of sputum negative TB.

PC-101313-13   External quality assessment of district controllers proficiency in AFB microscopy by panel test

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Rationale: There are more than 1100 microscopy laboratories and 90 intermediate district laboratories. >85% of districts are under external quality assessment (EQA) based on blinded rechecking of sample of smears examined at the diagnostic microscopy centers. Persistent difference in routine laboratory performance (very low positive in follow-up examination) and error identification (low number of HFN and LFN error) is observed between provinces PT was conducted to assess performance of controllers and effectiveness of EQA programme.

Material and methods: Panels were prepared by National Reference Laboratory (NRL). Each panel was comprised of sets of 10 stained and 10 unstained slides including 4 negative,4 high positive (two 1+, one 2+ and one 3+) and 2 low positives in each. Properly coded panels were sent to provincial reference laboratory (PRL) for onward transport to district intermediate laboratories by provincial supervisors. PT was conducted during on site visit, 135 intermediate lab staff in 85 districts were evaluated.

Result: Out of the total 135 controllers, 100% correct result were reported only by 21 (15.5%). 5/135 report HFP one or more HFN was reported by 43.0% (58) and one more LFP by 75.9% of controllers. Of all high positive slides 12.2% were reported as HFN and of all Low positive slides 43.5% were reported as LFN. Controllers (malaria supervisors) of Punjab province had lowest level of proficiency with 19.1% HFN and 57.7% LFN as compared to Sindh 7.6% HFN and 33.0% LFN.

Table   Laboratory performance versus EQA performance

	U. Punjab	S. Punjab	Sindh	NWFP	B-tan
EQA HFN	0.50%	0.70%	1.60%	0.80%	0.30%
EQA LFN	0.10%	0.10%	0.40%	0.20%	0.60%
PT HFN	23.80%	13.50%	7.60%	6.90%	3.10%
PT LFN	57.80%	57.70%	33.00%	33.90%	18.80%
F.UP SPR	1.77%	1.57%	5.63%	3.67%	1.39%
%DC with 0% +ve FUP	50.5%	42.7%	18.4%	43.8%	47.1%

Conclusion: Poor laboratory performance of peripheral lab staff associated with poor performance of controllers is responsible for low error identification in Punjab province. More intense supervision and on-job training of intermediate lab controllers especially those who are not regularly engaged in routine microscopy is required.

MDR-TB EPIDEMIOLOGY

PC-100864-13 Surveillance of antituberculosis drug resistance in Eastern Taiwan, 2004–2008

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Setting: A population-based surveillance of drug resistant tuberculosis (TB) in Eastern Taiwan, where the notification rate of TB was the highest in Taiwan.
Objectives: To investigate the pattern and trend of drug-resistant TB from 2004–2008 in Eastern Taiwan.
Methods: All culture positive TB patients whose isolates underwent drug susceptibility testing (DST) were enrolled. Drug susceptibility testing of first-line anti-TB drugs was performed. Results of the first isolate of each TB patient were analyzed.
Results: A total of 2689 culture-positive TB patients were detected. All of them were enrolled, of which 2179 (81.0%) were new cases and 510 (19.0%) were retreatment cases. Among new TB cases, the prevalence of any resistance, isoniazid resistance but not multidrug-resistant TB (resistant to at least isoniazid and rifampin, MDR-TB) and MDR-TB was 16.5%, 11.6% and 4.0%, respectively; and that among previously treated cases was 29.2%, 8.2% and 15.7%, respectively. The combined prevalence of all types of resistance decreased significantly from 2004–2008. The prevalence of any resistance among all cases was 22.2% in 2004, which decreased to 13.9% in 2008; and that of MDR-TB decreased from 10.4% in 2004 to 2.1% in 2008.

Table Prevalence of resistance to first-line anti-tuberculosis agents in eastern Taiwan, 2004-2008

Drug	All cases ($n = 2689$)	New cases ($n = 2179$)	Previously treated cases ($n = 510$)	P value	Odds ratio (95%CI)
	Number of isolates (percentage)				
Isoniazid	375 (13.9)	253 (11.6)	122 (23.9)	<0.001	2.39 (1.88–3.05)
Rifampin	186 (6.9)	97 (4.5)	89 (17.5)	<0.001	4.54 (3.34–6.16)
Ethambutol	40 (1.5)	23 (1.1)	17 (3.3)	<0.001	3.23 (1.71–6.10)
Streptomycin	245 (9.1)	188 (8.6)	57 (11.2)	0.072	1.33 (0.97–1.82)
MDR	168 (6.2)	88 (4.0)	80 (15.7)	<0.001	4.42 (3.21–6.09)

MDR = resistance to at least isoniazid + rifampin.

Conclusion: The prevalence of drug-resistant TB in Eastern Taiwan remained substantial. However, an effective TB control program has driven the prevalence of drug resistance downward.

PC-101403-13 Results of the Namibian tuberculosis drug resistance survey and implications for tuberculosis management

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Introduction: Namibia reported 13 332 tuberculosis (TB) cases in 2009; a high case notification rate of 634/100 000. 4602 (35%) were new smear positive cases while 3431 (26%) were retreatment. 356 drug resistant (DR) TB cases were reported in the same year (17 cases per 100 000). A TB drug resistance survey (DRS) was conducted in 2008 and data collection was completed in January 2009.
Design and analysis: This was a prospective study including all 34 districts in Namibia. PTB suspects presenting to health facilities between 1 May 2008 and 31 January 2009 had a survey form completed and sputum samples collected. Sputum smear positive (SSP) specimens were included in the survey. TB culture, drug sensitivity testing (C/DST) and an HIV test were performed on the sputum samples. Smear negative samples were excluded. Double data entry was

	New		Previously treated		Unknown		Total	
	Previous anti-TB history							
	n	%	n	%	n	%	n	%
Total patients with *Mycobacterium tuberculosis* and DST	1054	73	354	24	43	3	1451	100
Any resistance to isoniazid (H)	142	13.5	136	38.4	8	18.6	286	19.7
Any resistance to rifampicin (R)	48	4.6	78	22.0	3	7.0	129	8.9
Any resistance to ethambutol (E)	79	7.5	83	23.4	5	11.6	167	11.5
Any resistance to streptomycine (S)	102	9.7	106	29.9	8	18.6	216	14.9
Total monoresistance	98	9.3	59	16.7	6	14.0	163	11.2
Resistance to H only	58	5.5	33	9.3	3	7.0	94	6.5
Resistance to R only	4	0.4	9	2.5	1	2.3	14	1.0
Resistance to E only	16	1.5	9	2.5	0	0.0	25	1.7
Resistance to S only	20	1.9	8	2.3	2	4.7	30	2.1
Total multidrug-resistant TB (MDR)	40	3.8	58	16.4	2	4.7	100	6.9
H + R	4	0.4	6	1.7	0	0.0	10	0.7
H + R + E	0	0.0	3	0.8	0	0.0	3	0.2
H + R + S	6	0.6	13	3.7	0	0.0	19	1.3
H + R + S + E	30	2.8	36	10.2	2	4.7	68	4.7
Total polyresistance other than MDR	54	5.1	59	16.7	4	9.3	117	14.7
H + E	8	0.8	8	2.3	0	0.0	16	1.1
H + S	21	2.0	20	5.6	1	2.3	42	2.9
H + S + E	15	1.4	17	4.8	2	4.7	34	2.3
R + E	0	0.0	2	0.6	0	0.0	2	0.1
R + S	0	0.0	4	1.1	0	0.0	4	0.3
R + E + S	4	0.4	5	1.4	0	0.0	9	0.6
E + S	6	0.6	3	0.8	1	2.3	10	7.4

performed in Epidata version 3.1 and analysed in Epidata Analysis V.2.2.1.171.

Results: 1702 patients were recruited out of an intended 1800. Of these 1451 grew *Mycobacterium tuberculosis*. Any resistance to isoniazid (H) was 20% (95%CI 17.7–21.8) while any resistance to rifampicin (R) was 9% (95%CI 7.5–10.5). Resistance to H and R in retreatment cases was 38% (CI 33.5–43.6) and 22% (CI 18.0–26.6) respectively. Any multidrug resistant (MDR) TB was 6.9% (95%CI 5.7–8.3) while MDR–TB in new and retreatment cases was 3.8% (95%CI 2.8–5.1) and 16.5% (95%CI 13.8–20.8), respectively.

Conclusion: Resistance levels to H and R (including MDR-TB) among SSP patients are high. Namibia should consider rapid H and R testing for all SSP cases TB cases regardless of treatment history. In the absence of this testing, category 1 continuation phase should use R, H and Ethambutol due to initial high H resistance. A similar study should be considered using culture positivity as the inclusion criteria to give a more generalisable picture.

PC-101508-13   The true costs for patients to receive free TB and MDR-TB care

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Background: Tuberculosis (TB) treatment is ostensibly free to the population of Peru. However, TB patients often cite difficulty affording treatment as their main obstacle to treatment adherence. We investigated this paradox quantifying direct expenses incurred through treatment and indirect costs of lost income due to time spent away from work.

Methods: This was a prospective cohort study conducted in high TB incidence shantytowns in Lima, Peru. Patients who completed treatment between 2002 and 2009 ($n = 876$) were interviewed using a structured questionnaire regarding costs before and during treatment. Direct costs were defined as treatment-seeking expenditures. Indirect costs were defined as loss of household productive labour time for patients and family. Results were stratified between patients with drug susceptible ($n = 841$) and multidrug-resistant TB (MDR-TB) ($n = 35$). The unit of measurement used was the average per capita monthly income (MI) in TB-affected families, which was $36 US.

Results: The average total direct expenses prior to diagnosis were 4.5 MI, which comprised of 31% medicines, 5.8% natural remedies, 15% travel, 31% medical care, 17% food and 4.6% other costs. During treatment, average direct expenses were 4.6 MI and had a similar distribution except for greater
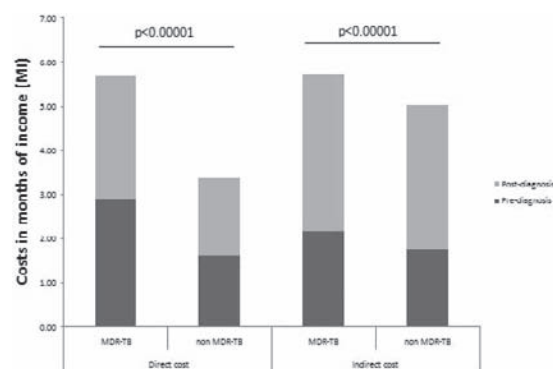
Figure   The costs for patient to receive free TB and MDRTB care.

travel expenses. The indirect cost of lost income was 3.9 MI prior to and 6.9 MI during treatment. Thus, the total direct expenses plus indirect costs of lost income prior to and during treatment combined was on average 19.9 MI per patient. Total costs were significantly greater for MDR-TB patients (11.5 MI) compared to patients with drug-susceptible TB (8.4 MI, $P < 0.0001$).

Conclusion: Even when diagnostic testing and TB treatment are provided free of charge, the direct and indirect costs to patients are high, especially for patients with MDR-TB. Economic support is likely to be necessary for poorer patients to be able to afford free treatment.

PC-100570-13   MDR-TB is bad enough: impact of second-line drug resistance on TB treatment outcomes in the US

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Background: The worldwide emergence of XDR-TB focused attention on treatment with second-line drugs (SLDs), however, the impact on treatment outcomes of resistance to individual SLDs is unknown.

Methods: We analyzed treatment outcomes among drug-resistant TB cases in the US national TB surveillance system, 1995–2006. We defined 3 patterns of first line drug (FLD) resistance: INH alone, INH+RMP, INH+FLDs other than RMP. We also defined 3 patterns of SLD resistance: fluoroquinolones (FQs) alone, injectables alone, and other SLDs. Using 2-way and stratified frequency tables, we compared treatment outcomes of cases having each pattern of FLD+SLD resistance with cases having the same FLD resistance but no SLD resistance. We used the χ^2 test, Fisher's exact test, and Mantel-Haenszel methods to determine statistical associations.

Results: Cases with resistance to INH or INH+FLDs other than RMP had signficantly better outcomes than cases with additional resistance to SLDs, e.g., INH resistant+FQ susceptible: 76% success vs. INH

resistant+FQ resistant: 64% success, $P < 0.0001$. In contrast, in cases with resistance to RMP or RMP+ other FLDs, outcomes were not significantly affected by SLD resistance, e.g., RMP resistant+FQ susceptible: 58% success vs. RMP resistant+FQ resistant: 54% success ($P = 0.3$). The same pattern held for second-line injectables and other SLDS. For all drug resistance groups, treatment success increased and death decreased after 1998. In parallel, outcomes were better for HIV-negative than HIV-positive cases for all drug resistance patterns.

Discussion: We expected SLD resistance to be associated with worse outcomes for all patients in whom SLD treatment was indicated. The results, however, suggest RMP resistance accounts for the majority of poor outcomes with modest contributions from specific SLDs. In HIV-infected cases, widespread use of highly active antiretroviral treatment after 1998 may have improved outcomes for all cases with drug-resistant TB.

PC-101294-13   Drug-resistant TB is an increasing problem in South Australia: a retrospective study

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Aim: To determine the incidence of drug-resistant *Mycobacterium tuberculosis* in the South Australian population and the associated demographic and microbiological characteristics.

Method: A retrospective study was conducted including all cases of *M. tuberculosis* diagnosed and treated in South Australia between January 2000 and December 2009. Demographic, clinical and microbiological data was collected and analysed.

Results: A total of 567 cases of *M. tuberculosis* cases were identified of which 48 had drug resistance to at least one of the first line agents (63%) or streptomycin (37%). The median age of patients was 33 (15–85), with 37% female. The majority of patients (91%) were born outside Australia; these patients migrated mainly from Africa (8.3%), East Asia (45.8%), Middle East (8.3%), South Asia (18.8%) and other regions (18.8%). The median time between arrival in Australia and notification of *M. tuberculosis* was 2 years (1 month 35 years). 48 isolates were resistant to at least one drug, of which 9 were multidrug-resistant tuberculosis (MDR-TB). All but one of the MDR-TB occurred within the latter half of the decade. 4 cases represented relapse of previously treated tuberculosis, of which 50% were found to have MDR-TB. 47 patients were successfully treated according to the current guidelines and 1 patient died from unrelated causes whilst on treatment.

Conclusion: Drug-resistant tuberculosis, especially MDR-TB is an increasing problem in South Australia. New therapies and public health strategies are necessary to control and prevent drug-resistant tuberculosis.

PC-100647-13   Second national anti-tuberculosis drug resistance survey in Myanmar, 2007–2008

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Objectives: To determine the prevalence of drug resistance to first line anti-tuberculosis drugs in new and previously treated pulmonary TB patients registered under National Tuberculosis Programme (NTP), Myanmar.

Method: A cross-sectional study was conducted at selected 40 townships using probability proportionate to size method. Required sample sizes for new smear positive and previously treated TB patients were 1479 and 691 after taking into account for expected loss for 15%. The study started in July 2007 and ended in mid 2008. For the study 1617 specimens were collected (1255 new and 362 previously treated). Out of which 1409 specimens were culture positive. 1370 isolates were tested for susceptibility to four first line anti-tuberculosis drugs except PZA.

Results: Of 1071 isolates tested from new TB patients, 6.4% were resistant to any one of the anti-tuberculosis drugs, 5.2% to isoniazid (INH), 4.9% to rifampicin (RMP) and 4.2% were multidrug-resistant (MDR). Of the 299 isolates tested from previously treated TB patients, 13% were resistant to any one of the anti-tuberculosis drugs, 11.7% to isoniazid (INH), 10.7% to rifampicin (RMP) and 10% were multidrug-resistant (MDR).

Conclusion: MDR among new TB patients increased from 4% to 4.2%, whereas MDR among previously treated TB patients decreased from 15.5% to 10% if compared to results of first nationwide drug resistance survey (2002–2003). Resistant to 4 drugs was increased and need to monitor periodically after introduction of 4 drugs fixed dose combination (INH, RMP, ETB, PZA) which has been in use since 2004.

PC-101370-13   Update on XDR-TB surveillance

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Background: As part of the efforts to monitor the development of drug resistance globally WHO routinely collects surveillance data on second-line anti-TB drug resistance, including extensively drug resistant TB (XDR-TB).

Intervention: Since 2002, 46 countries and 2 territories, distributed across the six WHO regions, have reported continuous surveillance or representative survey data on second-line drug resistance among MDR-TB cases. A total of 58 countries have reported at least one case of XDR-TB.

Results: Combining data from all 30 countries and 1 territory reporting at least one case of XDR-TB, the overall proportion of multidrug-resistant TB (MDR-TB) cases with XDR-TB, adjusting for the clustering effect at country level, was 5.4% (95%CI: 3.4–7.5). In 8 countries and settings with second-line drug susceptibility test results for more than 10 MDR-TB cases, the proportion of XDR-TB among MDR-TB cases was higher than 10% in Azerbaijan, Baku city (12.8%), Estonia (12.5%), Japan (30.9%), Latvia (14.8%), Lithuania (14.5%), South Africa (10.5%), Tajikistan, Dushanbe and Rudaki (21.0%) and Ukraine, Donetsk Oblast (15.0%). Of the 27 high MDR-TB burden countries, only 2 (Estonia and Latvia) routinely test MDR-TB cases for second-line drug susceptibility; 11 have not reported any cases of XDR-TB, which is more likely to be the result of lack of laboratory capacity than actual absence of XDR-TB strains.

Conclusions: The low numbers of XDR-TB cases reported in most settings make it difficult to establish the proportion of XDR-TB among MDR-TB cases. The overall proportion of MDR-TB cases with XDR-TB found by this analysis is in line with previous publications. As more and more patients with MDR-TB are diagnosed and started on treatment, collection and analysis of data on second-line resistance is of utmost importance for optimal patient care.

PC-101373-13   Association between MDR-TB and HIV status

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Background: Outbreaks of drug-resistant TB among people living with HIV have been widely documented in nosocomial settings. To date, limited information has been available about the association of HIV and drug-resistant TB at a population level.

Intervention: In 2008, 12 countries and 3 territories provided drug resistance surveillance data stratified by HIV status. Of them 9 countries reported at least one case of MDR-TB among patients with HIV-positive and HIV-negative status (Canada, Estonia, Georgia, Israel, Italy, Latvia, Mozambique, Republic of Moldova, and USA).

Results: In three Eastern European countries, Estonia (OR 2.4, 95%CI 1.0–5.3), Latvia (OR 1.9, 95%CI 0.9–3.5) and the Republic of Moldova (OR 2.3, 95%CI 1.6–3.3), HIV-positive TB patients appear to have greater risk of harbouring MDR-TB strains compared to HIV-negative TB patients. Similar findings have been documented in Mozambique. Given the large amount of missing HIV status data, it has not been possible to conclude whether an overall association between MDR-TB and HIV epidemics exists.

Conclusions: Although there appears to be an association between drug-resistant TB and HIV infection in some Eastern European countries, confirming what was already known from other settings in the same region, the data are still limited to be able to determine whether there is an overlap between the MDR-TB and HIV epidemics worldwide. Lack of an association between HIV status and MDR-TB in some settings can be due to low numbers of HIV-positive TB patients or patients with MDR-TB and consequent insufficient power in analysis. This may be a result of lack of testing of patients or of incomplete reporting of results. It is critical to include HIV testing in drug resistance surveys and in routine surveillance efforts in order to better understand the relationship between the two epidemics, which is key for optimal care of patients.

PC-100394-13   Review of drug susceptibility testing practices for TB re-treatment cases in Kenya

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Background: Multidrug-resistant tuberculosis (MDR-TB) threatens to reverse gains Kenya has made in achieving WHO TB control targets. However, the actual burden of MDR-TB remains unknown. TB re-treatment cases represent a cohort with the highest risk for MDR-TB. Standard clinical care for re-treatment cases includes drug susceptibility testing (DST) which, if optimized, could provide valuable MDR-TB surveillance data. In this study, we reviewed DST request practices for TB re-treatment cases in Kenya.

Methods: We reviewed national registration records of TB re-treatment cases in 2006 and compared these to DST data at the national TB central reference laboratory (CRL). A more in-depth audit was conducted in Nyanza Province and at the CRL to identify logistic obstacles that need to be addressed to optimize DST coverage.

Results: DST were performed for 2511 (24.4%) of the 10 462 TB re-treatment cases registered in 2006. Over the same period, Nyanza Province registered the lowest DST coverage rate of 10% (200 DSTs for 2000 re-treatment cases) compared to the other seven

Provinces. Nairobi Province registered the highest coverage rate of 53% (1238 DSTs for 2341 re-treatment cases). Several logistic obstacles accounting for the low coverage in Nyanza were identified. These included lack of basic supplies and standard operating procedures (SOPs), suboptimal field supervision, and communication gaps between regional TB clinics and the CRL.

Conclusions and recommendations: DST coverage for TB re-treatment cases is suboptimal and may lead to underestimation of the MDR-TB burden. As part of the efforts to improve the national MDR-TB surveillance system, Kenya must address logistic obstacles and expand DST coverage for TB re-treatment cases.

PC-100968-13   Tuberculosis drug resistant patterns: a review of routinely collected data

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Introduction: With the resurgence of tuberculosis (TB) disease in the late 1980s and early 1990s, multi-drug-resistant (MDR) TB has emerged as a serious challenge to TB control programmes. The aim of this paper was to describe the resistance patterns of MDR-TB in Botswana.
Methods: Data from 2006 to 2008 collected at national level in the MDR-TB registers was manually extracted. Records of MDR-TB confirmed by drug susceptibility testing and started on treatment were analyzed. Simple univariate analysis was done.
Results: A total of 219 laboratory confirmed MDR-TB records were retrieved. There were 118 males and 101 females. There was a significant difference in age between males (41.9 years) and females (32.5 years) with a P value < 0.001. Of the records reviewed, 7.8% had no history of previous of anti-TB treatment and 22.8% had a history of previous anti-TB treatment. A high proportion of 69.4% did not have any classification. HIV testing rate was 84.5%, and of these 77.6% HIV positive. Forty-seven (21.5%) had a 2 drug resistance pattern (i.e. RH), 75 (34.2%) had a 3 drug resistance pattern (i.e. RH + any other) and 97 (44.3%) had a 4 or more drug resistance pattern. Of the records with a classification of new, 52.9% had a 3 drug resistance pattern, while in the records with a classification of retreatment; 50% had a 4 drug resistance pattern. Only 5 records showed a history of isoniazid preventive therapy and 3 (60%) had a 3 drug resistance pattern. Twenty-two (22) patients had a treatment outcome of cured, 13 had completed treatment, 21 defaulted, 1 stopped treatment and 138 were still on treatment. Of the 19 records whose outcome was death, 70% were HIV coinfected.
Conclusion and Recommendation: Three or more drug resistance patterns are common in Botswana.

Poor recording may have affected our estimation of resistance patterns. Botswana is recommended to come up with a MDR-TB response plan.

TB IN LOW-BURDEN COUNTRIES

PC-100093-13   Risk factors for loss to follow-up of tuberculosis cases in England, Wales and Northern Ireland

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Background: Controlling tuberculosis (TB) depends on effective case management. Patients who are lost to follow-up are of large public health concern, as they may lead to further transmission and to development of drug-resistance. The aim of the study is to describe risk factors associated with cases being lost to follow-up.
Methods: We analysed data from the Enhanced TB Surveillance System in England, Wales and Northern Ireland, which collects information on the treatment outcome of new TB cases at 12 months. TB cases reported between 2001–2007 who were lost to follow-up at 12 months were compared with those who completed treatment or were still on treatment using univariate and multivariable logistic regression.
Results: Among 41 120 cases included in our study, 2410 (6%) were lost to follow-up, 36 768 completed treatment and 1942 were still on treatment. Men (OR 1.29, 95%CI 1.23–1.35), young adults (OR 2.37, 95%CI 1.78–3.17), patients with sputum smear positive pulmonary disease (OR 1.25, 95%CI 1.13–1.42) and those with missing information on previous diagnosis (OR 1.25, 95%CI 1.12–1.41) were at higher risk for being lost to follow-up on multivariable analysis. An interaction between length of residence and ethnicity was found: in all ethnic groups the highest risk was in recent entrants who arrived in the UK less than 2 years prior to diagnosis, with a larger effect seen in white (OR 6.43, 95%CI 4.50–9.21) than in Indian (OR 3.94, 95%CI 2.73–5.69), Pakistani/Bangladeshi (OR 3.01, 95%CI 2.04–4.45) and Black African ethnic group (OR 1.73, 95%CI 1.07–2.80).
Conclusion: In UK, the risk of becoming lost to follow-up is higher for young men with pulmonary sputum smear positive disease who entered the UK recently, this last risk being more pronounced among the white ethnic group. These patients might require enhanced case management and extra efforts should be put in place to prevent loss to follow-up. The role of ethnic group should be studied further.

PC-100352-13   Under-reporting TB in a university hospital in central Italy over ten years

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TB surveillance systems have several pitfalls outside of a National Tuberculosis Program and falling surveillance system hampers an accurate epidemiological quantification of TB. In Italy under-reporting TB is ranging from 12% (WHO 2003) to 37–54%. The present study wanted to quantificate TB burden in an University Hospital over a ten years period (1999–2008) and the quality of surveillance systems. Under-reporting assessment was done with record-linkage from 3 sources: National IX Infectious Diseases Surveillance (NDS) system, Hospital Discharge Records (HDR) of the University Hospital including any form of TB (International classification of Disease-IX TB code) and laboratory TB register (LR). A total of 787 pts were found. 580 pts were detected from HDR, 407 were from NDS register and 274 from LR: 326 (68%) pts with a discharge TB code were under-reported, 188 (32%) did not have a microbiological confirmation. We found a trend in all cases (98 in 1999, 44 in 2008) and a relative increasing of TB in immigrants (16 pts, 16% in 1999, 19 pts, 43% in 2008); under-reporting significantly changed (65% in 1999, 45% in 2008). In all populations, under-reported TB was 48%. There was a significant correlation with nationality (immigrants vs. Italians: 44% vs. 60%, $P < 0.005$), kind of diagnosis (microbiological confirmation: 35% vs. 55%, $P < 0.05$), kind of hospital regimen (inpatients vs. Day Hospital: 54% vs. 70%, $P < 0.05$), position of TB code in the discharge record (TB code in first position vs. in following position: 40% vs. 85% $P < 0.005$). A direct examination of medical records was done in 370 pts with TB code in first position, TB diagnosis was confirmed in 228 pts (62%), while in 210 pts with TB code in following position, TB diagnosis was confirmed in 42 pts (20%).
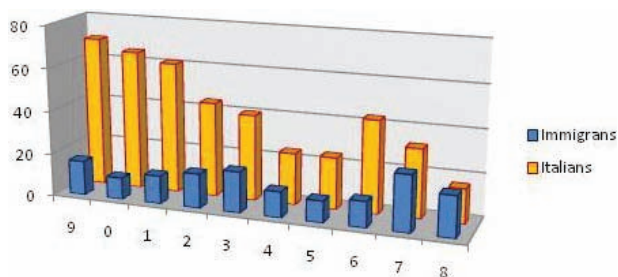
Conclusion: TB is under-reported, particularly in Italians and in pts without microbiological confirmation. The TB code in first position seems fairly accurate for confirming TB diagnosis.

PC-100407-13   Impact of immigration on tuberculosis epidemiology in a low-burden country

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Tuberculosis (TB) strains from 349 patients were isolated in Western Sweden during the years 2001–2005. Only 89 (26%) of the TB patients were born in Sweden. All the others were born in any of 42 different countries; 59 (17%) in Europe mainly Yugoslavia, 98 (28%) in Africa and 95 (27%) in Asia. The mean age of the Swedish patients was 67 years, while the mean age among the foreign patients was 37 years. The male/female ratio was 1.6 among the Swedes and 0.9 among those born abroad. Extra-pulmonary manifestations of TB were more common among African patients while lung infections alone were more common in Europeans. Spoligotyping showed that patients with strains of T or Beijing genotypes had more pulmonary TB than extra-pulmonary TB while patients with EAI and CAS genotypes had a high proportion of extra-pulmonary TB. The ancestral and/or evolutionary older PGG1 were more often found among the strains isolated from the foreign patients than among the Swedish patients who had strains generally being of the evolutionary recent genogroups PPG2/PPG3. We conclude that immigration from high incidence countries has strong impact on the TB epidemiology in Sweden. These findings should be taken into account by TB control strategists when developing programs for eradication TB in low prevalence settings.

PC-100803-13   Epidemiologic trend analysis: tool for monitoring tuberculosis elimination in low-incidence setting

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Many European Union (EU) countries have achieved tuberculosis (TB) incidences of fewer than 20 cases per 100 000 population with consistent 5-year declines in notification rate. They now need to consolidate their efforts and move towards the ultimate goal of eliminating TB. To monitor this phase in TB control, an important marker is the measure of ongoing transmission. Due to the lack of standardized methods to trace TB transmission in populations, surrogate

markers are needed. Analysing two countries with different TB incidences, we assessed the suitability of the following epidemiological trends as markers for monitoring progression towards TB elimination in the EU: 1) change in case notification rate, 2) change in ratio of notification rates in children and adults, and 3) change in mean age of new TB cases. These were adopted from the WHO Global Task Force on TB Impact Measurement and reflect both disease burden and levels of transmission. Between 1995 and 2007, Country A showed a steady trend in TB notification rates (40 cases/10 000 population). The ratio of notification rates in children under 15 years and adults increased during this period and the mean age among new TB cases decreased during the period. Although levels of notification remained steady (albeit high), the low age in TB cases suggest transmission was still ongoing in Country A. For the same period, the case notification rate in Country B fell from 55/100 000 in 1995 to just under 30/100 000 in 2007. The ratio of notification rates in children under 15 years and adults also decreased, supported by the increase in mean age of new TB cases. These trends suggest that the TB control programme strategies were successful in preventing transmission within the population. Provided that case surveillance and reporting system have a relatively high and stable sensitivity for capturing TB cases, these three indicators can provide a valid picture of the progress towards TB elimination.

PC-101061-13   Tuberculosis in Germany: do we reach a steady state?

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Background: Germany has a comparatively low tuberculosis (TB) incidence with a decreasing trend. Against this background, preliminary national TB data for 2009 were analyzed to identify how the epidemiological trend currently evolves.
Methods: Countrywide case-based datasets were collected via a national electronic reporting system (implemented in 2001) and analyzed by the Robert Koch Institute.
Results: From 2002 until 2008, total TB incidence rates have fallen from 9.3 to 5.5 per 100 000 inhabitants corresponding to an annual decrease ranging from 6.6 to 10.6%. For 2009 however, preliminary data reveal an incidence of 5.4 per 100 000 inhabitants (4432 cases) that is only a 2.3% decrease compared to the preceding year. TB incidence rates in children (<15 years) have fallen from 2.7 in 2002 to 1.1 per 100 000 children in 2008, showing an annual decrease ranging from 4.9 to 29.7%. For 2009, preliminary data show an increased incidence of 1.3 [95%CI 1.08–1.51; 143 cases] compared to the pre-

ceding year with an incidence of 1.1 [95%CI 0.93–1.34; 125 cases]. Yet, the corresponding increased relative risk of 6% is not significant ($P = 0.27$). The proportion of cases in children born in Germany remained stable in 2009 (68.5%, $n = 143$; 2008: 71.0%, $n = 124$).
Discussion and conclusions: Our observations for 2009 might serve as an early indicator for an approaching steady-state of TB incidence in Germany. The potential increase of pediatric notifications and the proportion of indigenous cases may indicate that ongoing TB transmission has not been reduced in 2009. Therefore, Germany, in line with other low-incidence countries, must be particularly vigilant in identifying and targeting sub-populations at risk of developing tuberculosis with timely and efficient preventive measures.

PC-101228-13   Risk factors for the misdiagnosis of tuberculosis

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Background: Following many years of decline, the number of tuberculosis (TB) cases in England, Wales and Northern Ireland has recently increased and the epidemiological picture has changed. Symptoms of TB are generic in nature and knowledge of the epidemiology of TB is an important factor in its diagnosis. We investigated the characteristics of cases initially diagnosed as TB and reported to national surveillance that were later found not to be TB to identify risk factors for misdiagnosis.
Methods: Enhanced Tuberculosis Surveillance collects demographic, clinical and treatment outcome data on TB cases in England, Wales and Northern Ireland. Reported cases may subsequently be denotified or reported as not TB following unsuccessful treatment and/or an alternative diagnosis. Risk factors for such misdiagnoses were assessed using multivariable logistic regression.
Results: Between 2001 and 2006, 46 840 cases were reported, of which 3784 (8.1%) were subsequently found not to be TB. On multivariable analysis, age groups 45–64 and 65+ years had 2.44 (95%CI 2.16–2.77) and 2.97 (95%CI 2.61–3.38) times the odds of misdiagnosis respectively compared to the 15–44 year age group and the white ethnic group had 2.78 (95%CI 2.25 to 3.43) times the odds of misdiagnosis compared to the Indian ethnic group. Pulmonary disease and being UK-born were also associated with an increased risk of misdiagnosis.
Conclusions: The groups at increased risk of misdiagnosis correspond to those groups where recent surveillance data indicate that the disease is now less common. The long-term reduction and the subsequent

change in epidemiology of TB in the UK may have led to less experience and knowledge of the current presentation of disease, leading to misplaced suspicion and misdiagnosis. The acquisition of specimens for culture confirmation is important in ensuring an accurate diagnosis, as well as full consideration of alternative diagnoses and current epidemiology.

TB IN SPECIAL POPULATIONS

PC-100165-13   TB genotyping to describe activation of LTBI among foreign-born persons in the US, 2004–2008

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Background: In the United States, the percentage of reported tuberculosis (TB) cases in foreign-born persons doubled, from 29% in 1993 to 58% in 2008. Small, geographically limited studies have suggested that most of these cases are due to the activation of latent TB infection (LTBI) acquired before U.S. arrival. Strategies for controlling TB due to activation of LTBI differ from strategies for addressing recent or community transmission: the former requires finding and treating LTBI; the latter requires interrupting transmission. We used a national data source to approximate the percentage of TB cases due to activation of remotely acquired LTBI and describe their characteristics.

Methods: Bivariate analysis was performed using national surveillance data on all TB patients with an isolate genotyped by the National TB Genotyping Service, 2005–2008. We defined a case of probable remotely acquired LTBI (PRA-LTBI) activation as active TB disease with a unique *Mycobacterium tuberculosis* genotype in a given county.

Results: Among the 26 711 genotyped patients 15 444 (58%) were foreign-born. PRA-LTBI activation was more common among foreign-born than among U.S.-born persons (70% vs. 55%, odds ratio [OR] = 1.88, 95% confidence interval [CI] = 1.78–1.97). Among foreign-born persons aged 15–44 at arrival, but not among other age groups, PRA-LTBI activation was more commonly diagnosed <2 years after arrival, compared with >5 years after arrival (OR = 1.57, CI = 1.42–1.74).

Conclusions: TB among foreign-born persons, compared with U.S.-born persons, may be more likely due to activation of LTBI acquired remotely. TB control strategies among foreign-born persons should focus on increased identification of LTBI prior to immigration and its timely reporting to US health officials, to ensure proper management upon U.S. arrival.

PC-100220-13   Healthcare workers in Rio de Janeiro's primary care TB clinics at risk for latent tuberculosis

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Aim: To estimate the prevalence of *M. tuberculosis* infection (LTBI) among healthcare workers (HCW) in primary healthcare units with TB clinics in Rio de Janeiro, a city with a TB incidence rate of 75.6/100 000 inhabitants.

Methods: After signing an informed consent, HCWs answered a questionnaire on demographic data, BCG vaccination, and place of work (TB versus other clinics) and were submitted to a tuberculosis skin testing (TST) using the Mantoux technique. LTBI was defined using two TST cut-off points: 5 and 10 mm.

Results: Among 71 included HCWs, TST was read in 67 (94%). All were BCG vaccinated, 75% at birth. Median age was 46 (21–73) years, 50 (75%) were female, 10 (15%) worked at the TB clinic. Overall LTBI prevalence using 5 mm and 10 mm as the cut-off was 22.4% (95%CI = 13.1%–34.2%) and 13.4% (95% CI = 6.3%–24.0%), respectively. Working at the TB clinic was the only variable associated with LTBI (50% × 17.5%; OR = 4.8; 95%CI = 1.1–20.9), considering the 5 mm cut-off value.

Conclusion: Occupational TB is a known risk among HCW and healthcare students but has been mainly documented in hospitals. We found a high prevalence of LTBI among primary care HCW, 5 times higher among those working in TB clinics. This finding suggests a high risk of infection in this setting, despite the small number of subjects included. The role of IGRA could not be assessed in this study, but our preliminary results suggest the need for periodical screening and treatment of recently acquired LTBI. A TST conversion study is ongoing among negative TST HCWs. Based on these preliminary results, TST seems to appropriately discriminate LTBI from BCG-attributable reactions.

PC-100386-13   The prevalence of multidrug-resistant *Mycobacterium tuberculosis* in a South African prison

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Background: Little information is available on the prevalence of MDR and extensively drug resistant (XDR) TB in South African prisons. This study reports on the drug susceptibility and genotype profiles of *M. tuberculosis* isolated from prisoners in a large prison between 2004 to 2007.
Method: Sputum specimens of prisoners presenting to the Health Care Facility at Durban-Westville Prison were routinely processed for smear microscopy, culture and drug susceptibility testing. The genotypes of 100 consecutive isolates for each year were identified by spoligotyping and IS*6110*-DNA fingerprinting.
Results: Drug resistance in culture positive cases was present in 60 (10%) of 607 in 2004, 89 (17%) of 516 in 2005, 44 (12%) of 371 in 2006, and 48 (13%) in 2007. Of these, MDR constituted 3.6%, 13%, 7.3%, and 6.8% respectively in each year. XDR TB was detected in one awaiting trial prisoner in 2006. The highest burden of MDR-TB, ranging from 54% to 88%, was consistently detected amongst the sentenced male prisoners. The predominant genotype infecting prisoners belonged to the Beijing family of strains. The F15/LAM4/KZN strain infected 2 patients each in 2005, 2006 and 2007. One of these exhibited a MDR phenotype in 2006.
Conclusions and recommendations: A four-fold increase in the prevalence of MDR-TB was observed from 2004 to 2005, after which it stabilized at approximately 7%. Infection prevention and control measures are of the utmost importance within this high risk population, more especially among the stable, sentenced male inmates. Active case finding is recommended to prevent spread of XDR-TB.

PC-100613-13   Global indigenous burden of TB: the unreported pandemic

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Aim: To describe indigenous peoples, 370 million in more than 70 countries, living in marginalized communities, with a high burden of health challenges, known levels of TB, association with low social determinants, life expectancy and access to care. To propose a Global Indigenous Stop TB Initiative to address the disparity.
Methodology: A literature review focused on indigenous peoples from Australia, New Zealand, Canada, the United States and Greenland was analysed to describe burdens of TB and links between social determinants and TB rates. Comparisons were made between indigenous and non-indigenous peoples in each country. The Global Indigenous Stop TB Strategy is proposed as a solution to consider.
Results: In industrialized countries for which disaggregated data are available TB rates are 6–185 times higher among indigenous peoples than among others born in those countries. Rates of change are better where program emphasizes treatment of latent infection. Rates of HIV as co-factor are not known.
Conclusion: More disaggregated data is needed to expand knowledge of indigenous TB. Testing of HIV in TB cases and TB in HIV in indigenous populations is critical. Studies linking social determinants to TB rates will form the basis of future interventions. Pilot studies addressing social determinants should clarify impact. A focal point will move the Global Indigenous Stop TB agenda and strategy forward.

PC-100814-13   TB among intravenous drug users in Georgia

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Background: IDU is widespread in Georgia and regardless of HIV status it is at increased risk of developing active TB. It is necessary to identify the screening and effectively address the TB cases among IDUs.
Objective: To assess the prevalence of TB among IDU-s through the screening programme.
Methodology: Using the data of prospective cohort study: from April 2008 to March 2009 IDUs at harm reduction and VCT sites were screened for TB symptoms with the questionnaire. TB suspect cases were referred to TB units for further investigation and diagnosis.
Findings: 3459 IDUs were screened for TB symptoms, 79 (2.3%) from them were female and 3380 (97.7%)—male, more than half (53.6%) were belonged to 30–39 age group. 81 (2.3%) from the screened IDU-s were HIV-positive and 2304 (66.7%) were diagnosed to have hepatitis B or C. 428 (12.4%) were classified as TB suspects. 381 (89%) suspected TB cases were presented at TB units for further examination. TB was diagnosed in 174 (45.7%) cases, 108 (62.1%) had pulmonary TB and 66 (37.9%) extra-pulmonary. The prevalence of TB among IDU-s was constituted to 5030/100 000 and was more than 40 times higher compared to general population.
Conclusions: IDU and TB represent a public health problem in Georgia, and stand high risk of TB. Active case finding is one of the useful tools for addressing TB problem among this group.

PC-100894-13   Infection control and burden of tuberculosis infection and disease in health care workers in China

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Aim: To assess tuberculosis (TB) infection control practices, and the prevalence of TB infection and TB disease and risk factors in health care workers (HCW) in TB clinics in China.

Methods: Cross-sectional survey of TB clinics and their health care workers in Henan province in China in 2005.

Results: The infection control practices assessment showed that the patient consultation areas and X-ray areas were in separate rooms from the waiting area and administrative area in a minority of the clinics. Mechanical ventilation was not available in any TB clinic. N95 respirators were not available for HCW and surgical masks were not available for TB patients and suspects. Twenty cases of pulmonary TB were detected among the 3746 HCWs. The prevalence was 672/100 000 among medical staff and 247/100 000 among administrative/logistic staff. Employing a tuberculin skin test (TST) induration size of 10 mm as the cut-off point, the TB infection proportions in those with and without BCG scar were 55.6% (432/777) and 49.0% (674/1376), respectively ($P = 0.003$). HCWs at increased age, with higher educational background, longer duration of employment, and working at the prefecture level had higher TB infection prevalence. Administrative/logistic staff and pharmacy staff had the lowest prevalence of infection.

Conclusion: TB infection control in TB clinics appears inadequate and the prevalence of TB infection and disease among HCW is high. TB infection control practices in TB clinics should be strengthened in China, including renovation of buildings, and use of respirators and masks. Moreover, regular screening of HCW for TB disease and infection needs to be considered, offering preventive therapy to those with TST conversions.

PC-101187-13   Evaluation of clinical prediction rules for tuberculosis in emergency settings

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Background: As nosocomial transmission of tuberculosis continues to be a public health challenge in many countries, methods for optimization of respiratory isolation of tuberculosis suspects should be assessed. Several clinical prediction rules (CPRs) for pulmonary tuberculosis (PTB) have been published and can be used in emergency settings. We evaluated their performance in the emergency room of a hospital with a high prevalence of tuberculosis in Lima, Peru.

Methods: We performed a literature search to identify CPRs to predict PTB that could be used in emergency settings. We applied the selected ones on a dataset containing clinical, radiographical and microbiological data from 345 patients attending an emergency room with respiratory complaints in Lima, Peru. Each CPR was applied to every patient and the results were compared with culture as a reference standard for diagnosis of tuberculosis. Sensitivity, specificity and predictive values were calculated for each CPR, and ROC curves for those consisting in scores.

Results: We found 13 CPRs to predict PTB. The CPR performing the best was Mylotte's one, attaining an area under the ROC curve of 91%, a sensitivity of 88.9% (CI 85.6–92.2) and a specificity of 63.9% (58.8–69.0). The others had suboptimal performance. The results of 2 consecutive sputum smears attained a sensitivity of 75.6% and a specificity of 99.7%.

Conclusion: Only one of the 13 CPRs evaluated (Mylotte's), could be considered a useful tool to help on the decision of isolation of patients with clinical suspicion of PTB. It was more accurate than the results of 2 sputum smears alone to decide on respiratory isolation. In a setting with 30% of PTB prevalence among suspects, this would mean a reduction of isolation rates to less than half of rates based on CDC recommendations, at the expense of missing very few infectious patients. Nevertheless, we recommend local validation before its wide application.

PC-101302-13   Prevalence of pulmonary tuberculosis among prisoners and jail officers in the Philippines

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Background: The prevalence of TB in prisons is reportedly ten times higher than that of the general population. No local study has been done to determine the magnitude of the TB problem in prisons. Thus, this study was conducted to estimate the prevalence of bacteriologically confirmed pulmonary TB (PTB) and culture-based multidrug-resistant TB (MDR-TB) among prisoners and jail officers in the Philippines.

Methods: There were 2117 inmates (69.5% male; 30.5% female) and 549 jail officers from 7 selected

prisons; all underwent chest radiography and interviewed for TB symptoms. Those with either confirmed radiographic findings or chronic cough of at least 2 weeks underwent direct sputum smear microscopy and TB culture. Those with (+) culture for *M. tuberculosis* underwent drug sensitivity test (DST).
Results: Among inmates, 53% were TB suspects based on symptoms (28%) and suggestive chest X-rays (42%). Prevalence of bacteriologically-confirmed PTB per 1000 defined as at least 2 AFB (+) sputum and/or (+) culture for *M. tuberculosis* is 27.2 among males (95%CI 23.7, 30.7) and 4.6 among females (95%CI 3.2, 6.1). Of the 9 with DST results, 2 were confirmed MDR-TB based on resistance to isoniazid, streptomycin and rifampicin; 1 was resistant to isoniazid only. 64 (12%) of jail officers were TB suspects; only 37 submitted sputum specimens which were all negative.
Conclusions: The prevalence of bacteriologically confirmed TB among prison inmates, particularly the males, is almost 7 times higher than that of the general population. Because of the infectious nature of bacteriologically-confirmed PTB, serious prevention and control measures must be installed to avoid transmission to the jail officers and to the visiting community. Aside from treatment of cases, early detection through cough surveillance and thorough physical examination of inmates upon entry and before release to the community must be done.

PC-100567-13 Follow-up of patients under MDR-TB treatment after release

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Aim: Launching a pilot project to follow up Drug-Resistant TB patients after release from prison while under treatment and develop a sustainable strategy on follow-up.
Methods: A Memorandum of Understanding was signed on March 2009 between MOH, MOJ and ICRC on piloting follow-up of the first 20 DR-TB patients after release from prison TB hospital without completing their MDR-TB treatment.

A health staff is assigned and is issued monthly incentives to provide follow-up of treatment. Every month sputum and blood specimens are collected from each transferred-out patient and transported to prison laboratory for smear, culture, DST and biochemical analyses.
Results: Since April 2009 up to March 2010, 20 MDR-TB patients were released from prison and 18 of them provided with continuation of treatment, while 2 discontinued their treatments. Out of 18 transferred-out patients, 2 successfully completed treatment, 2 defaulted and 14 are still under treat-

ment. The bacteriological status of the 18 patients is as follows:

12 were and remained ss- cc- before and after release (2 cured and 1 defaulted)
4 were ss− cc+ before release and became ss− cc− after release
1 was ss− cc+ before release and became ss+ cc+ after release
1 was and remained ss+ cc+ before and after release (defaulted)
The cost of these joined follow-up activities of the released prisoners has been calculated and it is as follows:
1 patient from the Baku city area costs 115 USD per month
1 patient from the rural area costs 367 USD per month
Conclusion: Project shows significant success since the vast majority of the released patients can be followed-up in order to continue their treatment. As it is shown by the comparison of the cost calculation, it would be more appropriate to involve in the future primary health care structures in the project and by doing so to decentralize the treatment monitoring procedures.

PC-100837-13 Prevalence of diabetes amongst tuberculosis patients in Kerala, South India

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Background: Diabetes mellitus is extremely common in the southern Indian state of Kerala (population 34.6 million), with a community prevalence of 17%. Diabetics are immuno-compromised to varying degrees, and have a higher risk of tuberculosis (TB) than non-diabetics. Routine screening for diabetes amongst TB patients may be a way to identify previously undiagnosed diabetes, offer optimum diabetic care and may reduce long-term morbidity. A study was conducted to estimate the prevalence of diabetes amongst TB patients registered under the Government of India's Revised National TB Control Programme (RNTCP) in Kerala.
Methods: In 9 of 14 districts of Kerala (population 25 million), all patients over age 15 years registered as TB cases under RNTCP from October to December 2009, were screened for diabetes routinely by TB service providers. Diabetes was defined as those persons having fasting blood sugar of 126 mg/dL or more, and/or random blood sugar of 200 mg/dL or more, as per the Indian Diabetic Association guidelines.
Results: Of 4186 registered TB cases aged 15 years and above, TB service providers successfully screened

2734 (65%) for diabetes. A total of 703 (26%) of the screened TB patients were found to be diabetic. The median age of those found to be diabetics was 49 years (range 16–85). The highest age-group specific prevalence was amongst patients aged 55–64 years, where 30% of patients were diabetic. There was no difference in the prevalence of diabetes between new cases (26%) and re-treatment cases (29%) overall.

Conclusion: Up to one-quarter of TB patients registered under RNTCP in Kerala may be diabetic, many of whom were previously undiagnosed. In Kerala, adults with TB should be routinely screened for diabetes and linked to appropriate diabetic care.

TB PROGRAMME: MONITORING AND EVALUATION

PC-100257-13   Controlling TB and limiting drug resistance in 3D: default, diagnostics or drugs?

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Drug resistance has made the control of TB more difficult. Current plans to achieve global TB control emphasize the development of new diagnostic tools and novel drugs that are efficacious in the presence of drug resistance. The primary objective of the study was to compare expected TB related outcomes (including drug resistance), over 20 years, with different control scenarios. Scenarios included 1) DOTS, 2) improved treatment completion by reducing default rates, 3) improved case finding and 4) the addition of novel drugs effective for all types of TB cases, including those that are drug resistant. A Markov state transition model that included a transmission component and initial and acquired drug resistance was developed. Mean global data were used. Key pathogenetic and epidemiologic probabilities were taken from published sources. Outcomes predicted included annual estimates of the risk of TB infection, TB related deaths and the number of new TB cases, in each of the four categories of drug resistance: susceptible, single drug-resistant (SDR), poly drug-resistant (PDR) or multidrug-resistant (MDR). Sensitivity analysis on initial drug resistance level was conducted. With DOTS alone, 1928 TB deaths and 5590 TB cases were predicted over 20 years, per 100 000 population. Approximately 4% of cases were predicted to be MDR. When default rates were improved, a small reduction in deaths and cases resulted. When case detection was maximized deaths and cases were reduced by almost 70% and 10%, respectively, with only a small increase in MDR (<1%). When novel drug regimens were considered, small reductions in TB deaths and cases were predicted, but the number of MDR cases was reduced by more than 20%. The development of new drugs will remain an important strategy for the treatment of drug resistant cases, especially for those that are MDR. Case detection should remain the focus of TB control programs if success is measured through reduced mortality.

PC-100713-13   Treatment outcomes and current status of category II TB cases in Botswana

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Background: Patients who fail category II TB treatment have a high risk of multidrug resistant TB (MDR-TB). The aim of the study was to determine the current status of patients who started Category II treatment in Botswana between January 2004 and December 2007, whose outcome was reported as default, failure or unknown.

Methods: We used the electronic TB register (ETR. Net) to identify patients with category II treatment outcomes of default, failure or unknown, then reviewed treatment and medical records to determine the current status of these patients. Descriptive statistical analysis was applied.

Results: A total of 523 patients' records were retrieved from the ETR.Net of whom there were 325 (62%) males and 198 (38%) females. The median age was 32 years (SD 16.4). Of 173 patients with an HIV test result, 166 (31.7%) were positive. According to the ETR.Net, 375 (72%) patients had an unknown treatment outcome; 96 (18.4%) were defaulters and 52 (10%) were failures. Review of the paper records however showed that the actual outcomes of these 523 patients were unknown 90 (17.2%), defaulted 63 (12.0%), failures 19 (3.6%), completed 134 (25.6%), cured 57 (10.9%), died 56 (10.7%), transferred out 92 (17.6%), physician stopped treatment 2 (0.4%) and started MDR-TB treatment 10 (1.9%). The predictive value (PV) for ETR.Net was 24% for unknown, 65.6% for defaulter and 36.5% for failure.

Conclusions: There is considerable misclassification of treatment outcomes in Botswana. The national TB control program should strengthen recording and reporting practices by health care workers.

PC-100311-13   Global reporting on enrolment of MDR-TB patients on treatment and their outcomes

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Background: It is estimated that 440 000 MDR-TB cases emerge each year in the world. In order to assess the global response to the challenge of drug-resistant TB, WHO collects information about enrolment of MDR-TB patients on treatment and their outcomes.

Intervention: Countries report outcomes of patients to WHO using standard aggregated tabulation. Latest data on treatment outcome relate to 2006, given that final cohort reports are collected at least 24 months after the start of treatment. They include data from Green Light Committee-approved projects. Reports without prior patient treatment history or where >20% of cases were still on treatment at time of report were excluded.

Results: Sixty-three countries or territories reported outcomes for patients enrolled in 2006, while another eight had data from 2004–2005. A total of 4500 treatment episodes were included, representing 11% of the MDR-TB cases expected to occur among TB cases notified by these countries 8% of new and 14% of previously treated. After adjusting for clustering effect by country, overall treatment success was 60% (95%CL 55–66%) and 12% (9–14%) of cases died. Outcomes were not significantly different between new cases and retreated cases (Table).

Table   Outcomes of MDR-TB cohorts

	New			Retreated			
	n	%	95%CL*	n	%	95%CL*	Total
Success	1024	64%	56–73%	1626	56%	41–70%	2650
Died	130	8%	6–11%	352	12%	8–16%	482
Failed	125	8%	3–12%	338	12%	4–19%	463
Other**	310	20%	14–25%	595	20%	16–25%	905
Total	1589			2911			4500

* Robust standard errors approach used to estimate confidence limits.
** Includes default (66%) and other cases without follow up information.

Conclusions: Reports on enrolment of MDR-TB patients on treatment and their outcomes remain very incomplete. The likelihood of treatment success for MDR-TB patients remains low as a result of a high risk of dying, of failed treatment or of the interruption of prescribed treatment the duration of which with current regimens may last 2 years or more.

PC-101385-13   Progress in reaching milestones for drug resistance surveillance in the Global Plan to Stop TB

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Introduction: A milestone for 2010 in the Stop TB Partnership's Global Plan to Stop TB 2006–2015 is that representative and reliable data on anti-TB drug resistance should be available from 130 countries, including all countries with a high burden of TB, MDR-TB, and/or TB-HIV, with half reporting trend data (2 or more data points). The milestone also calls for revised estimates of the global MDR-TB burden to be published. In this abstract, progress in reaching the 2010 milestone for global drug resistance surveillance is evaluated, and remaining gaps are identified.

Methods: Analysis of data collected from representative surveys or surveillance systems and provided by countries to WHO as part of the Global Project on Anti-Tuberculosis Drug Resistance Surveillance.

Results: As of March 2010, 114 out of 193 countries globally, 21 of the 27 high MDR-TB burden countries, 18 of the 22 high TB burden countries, and 26 of the 41 priority TB-HIV countries had provided data (see Table). However, when considering only nationwide and recent (i.e. less than 10 years old) data, only 13 of the 27 high MDR-TB burden countries, 10 of the 22 high TB burden countries, and 13 of the 41 priority TB-HIV countries had provided data. Trend data were available from only 55 countries, most of which were not high burden. In 2010, WHO estimated that between 390 000 and 510 000 MDR-TB cases emerged globally in 2008 (best estimate 440 000 MDR-TB).

Indicator	Global Plan milestone for 2010	As of March 2010, cumulative countries providing data since 1994
Representative anti-TB drug resistance data, all countries	130	114
22 high TB burden countries	22	18
27 high MDR-TB burden countries	27	21
41 high priority TB-HIV countries	41	26
Time trend data, all countries	65	55
22 high TB burden countries	11	7
27 high MDR-TBburden countries	14	8
41 high priority TB-HIV countries	21	10

Conclusion: Although falling short of the 2010 milestone, the number of countries with drug resistance data is growing. Laboratory capacity and logistic obstacles, including the cost of surveys (on average over US$100 000), have prevented the organization of surveys in a number of settings. Current efforts to

strengthen laboratory networks will likely accelerate the implementation of surveys and ultimately the establishment of continuous surveillance systems.

PC-100135-13   Progress of Nepal's multidrug-resistant TB programme on completion of four years: lessons learnt

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Background: Nepal's National Tuberculosis Control Programme has managed a Green Light Committee-approved DOTS Plus project since 2005, using standardized treatment regimens and a predominantly ambulatory approach. The project offers treatment from 10 treatment centres and 34 treatment sub-centres throughout the country. We undertook to review the outcomes from the first four years of the program.
Methods: Free, standardized treatment (kanamycin, ethionamide, cycloserine, pyrazinamide, ofloxacin) is provided for category 2 failures and other culture-demonstrated multidrug-resistant cases. Monthly

Figure   MDR TB management program sites in NTP and partner organizations.

medical reviews include smear and culture testing, and serum monitoring for potassium and creatinine. Outcomes were recorded according to the standard Laserson definition.
Results: By the end of 2009, 681 patients were enrolled. The largest number of MDR-TB cases registered were failures of CAT 2 (90%), followed by CAT I failures with culture and DST confirmed MDR (5%). Complete outcomes were available for 376 patients who started treatment from 2005 through 2007, with the following results: cure (65%), default (18%), failure (7%), death (10%). Preliminary data suggests that the default rate fell among patients who started treatment in 2008 (6% by end of 2009), following provision of a monetary stipend for patients (approximately 20 USD per month).
Conclusion: Cure rates for Nepal's DOTS Plus programme remain on par with international standards. Default rates have been high, particularly among patients from rural areas, who incur significant travel, living, and indirect expenses to receive treatment. Providing economic support may reduce default and improve outcomes for MDR-TB in low-income settings.

PC-100481-13   Alignment of Global Fund Round 6 through 9 TB proposals to the Stop TB Strategy

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The Global Fund provides 63% of external funding for TB control efforts. The approved 5 year upper ceiling TB amounts are: US$493 million in R6, US$364 million in R7, US$856 million in R8, and US$1.48 billion in R9. The Stop TB Strategy has 6 components: 1) Pursue high-quality DOTS; 2) Address TB-HIV, MDR-TB and other challenges; 3) Contribute to health system strengthening; 4) Engage all care providers; 5) Empower people with TB and communities; 6) Enable and promote research. An analysis of the budgets according to Stop TB Strategy service delivery areas was conducted for TB proposals from round 6 through 9. Two proposals are not included in the analysis due to unavailability of comparable data. The Stop TB Department, World Health Organization, developed Stop TB Planning Matrix and Framework to help countries plan all components of the Stop TB Strategy in line with the Global Plan to Stop TB 2006–2015. TBTEAM, the TEchnical Assistance Mechanism of the Stop TB Partnership, facilitates technical assistance to countries for proposal preparation and implementation. The budget distribution by Stop TB component was 1) R6 = 52%, R7 = 47%, R8 = 59%, R9 = 55%; 2) R6 = 22%, R7 = 33%, R8 = 25%, R9 = 32%; 3) R6 = 3%, R7 = 4%, R8 = 7%, R9 = 2%; 4) R6 = 3%, R7 = 2%, R8 = 1%, R9 = 2%; 5) R6 = 18%, R7 = 7%, R8 = 8%, R9 = 8%; 6) R6 = 2%, R7 = 1%, R8 = 1%, R9 = 1%.
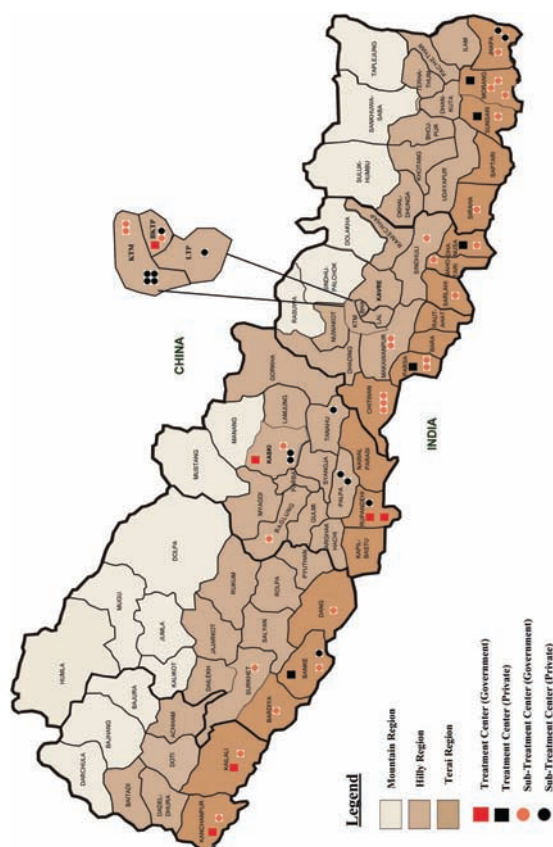
TBTEAM technical assistance for proposal preparation and the alignment of Stop TB planning and budgeting tools with Global Fund Monitoring & Evaluation Toolkit, Performance Framework and Enhanced Financial Reporting, helped to ensure successful TB proposal submission (62% in R6, 51% in R7 and 8, and 60% in R9). To ensure similar success in future rounds and successful implementation alignment is extended to the promotion and use of the WHO Stop TB Planning and Budgeting Tools as a way to establish national strategic plans, monitor progress towards the targets as set out in the Global Plan to Stop TB and facilitate monitoring expenditures.
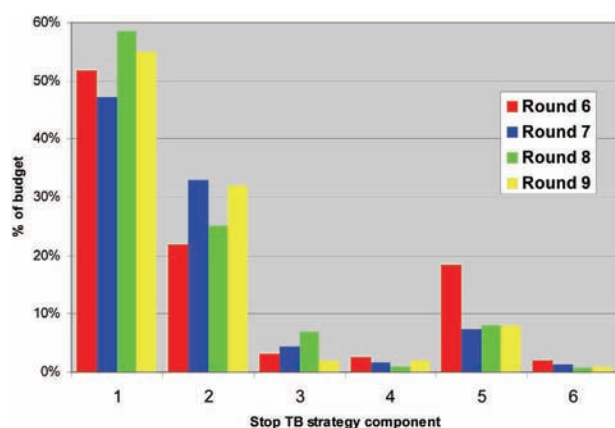
Figure   Budget distribution by Stop TB component and round.

PC-100960-13   Drug procurement through the Green Light Committee mechanism: lessons learnt implementing DOTS Plus Projects in Russia

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Objective: To define the main problems of second-line drug (SLD) procurement through the Green Light Committee (GLC) mechanism taking into account the experience of the Global Fund (GF) R4 TB Program in Russia.

Introduction: Since 2005 GF R4 TB Program has been implemented in Russia (6000 MDR-TB patients enrolled). Certain problems with the drug procurement through GLC mechanism became the main obstacle to smooth implementation of the Program and seriously delayed the start of enrollment of patients.

Results: GF R4 TB Program in Russia faced the following problems:
1 Suppliers of second-line TB drugs authorized through GLC are not registered in Russia.
2 Ongoing administrative reform in Russia in the field of drug registration, customs and humanitarian aid regulations.

3 Miscommunication among participating national and international partners.
4 Lack of reliable method of assessment of drug needs for numerous project sites working within one Program with huge total number of patients treated.

The above problems resulted in extremely long and unpredictable time of procurement, menace of shortages, as well as the constant need of redistribution of the drugs among the projects in conditions of strict system of national humanitarian aid regulation. The problem of communication during the first two years of the Program was solved only through mutual visits and creation of the crisis team. Only in face-to-face discussions the parties managed to elaborate realistic response to existing challenges. During Program implementation RHCF in cooperation with WHO RUS invent the own method of drug needs calculation adapted to Russia.

Conclusion: The global problems to be addressed:
1 Only one supplier with limited range of products for GLC projects.
2 GLC mechanism has to be compliant with national drug regulations.
3 Proper tools and expert support in area of assessment of drug needs in huge projects, training of relevant staff.

PC-101521-13   Monitoring tuberculosis program progress in the United States: the national tuberculosis indicators

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Aim: Monitoring and evaluation are often perceived as an added burden. We maximized the use of surveillance data and developed the National Tuberculosis Indicators Project, a web-based performance monitoring system to help programs track progress, and prioritize efforts for improvement.

Method: CDC and partners selected 15 national objectives highlighting priority activities and outcomes for TB control. Standardized indicators and reporting templates were designed to provide clear, simple depictions of epidemiologic and programmatic data with 5-year trends (most recent years with complete data for the indicators). Program officials receive indicator reports online.

Results: Nationally, most indicators of TB case management improved between 2004 and 2008. However, treatment completion rate for patients with TB remained unchanged while the reporting rate of the initial drug-susceptibility test results decreased. HIV status reporting increased across all age groups, reaching 79.8% of TB cases with status reported in 2008. TB cases reported having refused HIV test, not offered

the test or with unknown or missing data have also decreased. Results for contact investigation indicators are mixed from 2002 to 2006. Performance on medical evaluation of contacts to infectious cases decreased from 82.2% to 79.6%, while the latent TB infection treatment completion rates improved from 59.1% to 65.6%.

Conclusion: The results summarize national progress toward objectives. Program managers are encouraged to compare their performance against the national trend, and to formulate plans to address individual program barriers. NTIP reinforces national priorities, outlines an approach to program improvement and technical assistance, and provides data to support evidence-based program planning.

POSTER DISPLAY SESSIONS

ACCELERATING TB-HIV PROGRAMME ACTIVITIES: LTBI/DOTS/ QUALITY IMPROVEMENT

PS-100244-13   Strategic actions to address progress of drug-resistant TB: beyond DOTS

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Background: TB is the leading infectious killer of HIV positive people in the developing world which includes Kenya. Drug-resistant TB is threatening progress in the fight against HIV/AIDS. 86% of people with tuberculosis who are HIV-positive are 50 times more likely to develop active TB than HIV-negative. XDR-TB is on increase while 49% are all positive. Efforts in combating TB is through partnerships at the country level engaging non-governmental organizations, community, FBO's, to strengthen, implement effective TB-HIV programs. Public hospitals remain the only option for 'high risk' groups to receive TB health services but hidden costs excludes them from receiving timely services though medication is free.

Methods: Study was conducted through qualitative method to explore perceptions of TB-HIV managers on implementation of TB-HIV collaborative activities, identified barriers for provision of TB-HIV integrated care. 7 semi-structured interviews with district TB, HIV co-coordinators at PGH. Patient survey, focus group discussion, qualitative interviews.

Results: 49/54 (86%) clients who's compliance of TB drug treatment was 'ideal' and scored 'high' receiving 4–9 social interventions during the course of treatment. In the 'ideal' compliance group 47% regularly attended clinic while 42% were mainly outreach. Group requiring outreach had lower social

intervention scores. Social interventions correlate with medication compliance rates. NLTP initiated innovative early detection, prevention targeting individuals infected with HIV. Barriers identified included high case load, inadequate collaborative programme, clinical management trainings on HIV-TB, physical layout of TB-HIV services, nurses de-motivation, stigma.

Conclusion: Innovative ways to deliver health within the prevailing economic context. Behavioral research to enhance correct use of TB-HIV prevention strategies. New drugs, more lab capacity needed to diagnose, treat TB-HIV co-infection. Improve policy of urbanization.

PS-100889-13   The DOTS strategy and ART in pulmonary TB-HIV co-infected patients

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Background: The study was conducted to evaluate efficiency of providing combined ART and DOTS I, DOTS II therapy to PTB-HIV co-infected patients with or without hepatitis B, C and OIs.

Design/methods: We evaluated 75 patients who had ever received PTB treatment and were under follow-up at the National AIDS Center in the period of 01.01.2005–01.01.2009. The patients under survey were divided into two groups: I group the patients who, due to some reasons, did not receive ART ($n = 55$), II group the patients receiving ART ($n = 20$).

Results: Twenty-one patients from I group treated by DOTS I died, 12 of them had been diagnosed with hepatitis B and C and/or OIs. Eight patients died in the initial phase of the therapy. Nine of the 13 patients treated by DOTS II died in the initial phase of the therapy, of whom 9 were diagnosed with hepatitis B and C and/or OIs. Three patients with MDR-TB also died. One of the 15 patients from II group treated by DOTS I died, and 14 underwent full course of TB treatment and continue to receive ART. Of them 12 were diagnosed with hepatitis B and C and/or OIs. Four patients treated by DOTS II, underwent full course of TB treatment and continue to receive ART. One of them was diagnosed with hepatitis C, 3 with OIs. One patient with MDR-TB died. The obtained results demonstrate that total death rate in the I group of patients not receiving ART, was 60%. Total death rate in those receiving ART, was 10%. Average CD4+ cell count in the I group patients is higher, and occurrence of hepatitis B, C and OIs are nearly the same in the both groups. Thirteen patients from I group died in the DOTS I continuation phase, 9 died in the DOTS II initial phase. 90% from the II group, receiving ART, were successfully treated by DOTS I, DOTS II.

Conclusion: The study results show significant improvement of survival in patients with PTB-HIV

co-infection receiving combined ART and DOTS I, DOTS II therapy.

PS-101134-13   Effect of INH preventive treatment in HIV patients of PPD+

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Objective: There has been little study of INH preventive treatment in HIV patients in China despite many years' research in developed countries. The paper is to investigate effect of preventive treatment INH treatment in HIV patients of PPD+.
Method: In Hibei province's 13 counties/districts with high HIV infections, questionnaire survey, CD4 counting, PPD tests, X-rays and sputum tests were done in people living with HIV. INH treatment was conducted in HIV patients/people infected with HIV for 9 months and TB was diagnosed after 1 year.
Result: There were 191 non-TB cases of PPD+ in 1071 HIV cases. 167 patients agreed but 24 refused to receive 9-month INH treatment One year later, diagnosis found one TB case in the 167 patients with INH treatment, the yearly TB rate 0.65%: 3 TB case in the 24 patients with no treatment, the yearly TB rate 12.5% ($\chi^2 = 14.5$, $P < 0.05$).
Conclusion: INH preventive treatment is effective in reducing TB cases in HIV patients of PPD+.

PS-100685-13   Low risk of hepatotoxicity in a trial of community-wide isoniazid preventive therapy in South Africa

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Background: Hepatotoxicity is the most serious among potential adverse effects of isoniazid preventive therapy (IPT). We describe the frequency of and risk factors for hepatotoxicity in Thibela TB, a cluster-randomised study of community-wide IPT among gold miners in South Africa, a setting of high HIV prevalence.
Methods: Consenting employees in intervention clusters were screened for active tuberculosis and higher risk of isoniazid toxicity (including history of chronic liver disease; symptoms suggesting active hepatitis; alcohol intake >28μ/week (>21μ for women); pregnancy or <3m post partum; and concomitant medication increasing risk of hepatitis) using a questionnaire and chest radiograph. Participants were educated to report to study staff in the event of symptoms suggesting hepatitis: liver function tests were only performed if clinically indicated. All deaths among individuals taking IPT were reviewed for possible adverse events.

Results: Among 24 202 participants starting IPT (95.2% male, median age 40 years), 17 (16 male, median age 42 years) experienced clinical hepatitis (0.07%), a median 117 (IQR 30–177) days after IPT start. Two cases fulfilled criteria for seriousness, including one death. 2/17 were more likely due to a cause other than IPT. Among 15 cases at least possibly attributed to IPT, there was no evidence of association between hepatotoxicity and sex, age group, weight or concurrent antiretroviral therapy. Individuals reporting any alcohol consumption (vs. none) were more likely to experience clinical hepatotoxicity though the overall risk was very low (0.11% vs. 0.3%, odds ratio 3.9 [95%CI 1.2–12.1]).
Conclusions: The risk of hepatotoxicity was very low in this population despite a relatively high median age. Our data suggest that clinical criteria can safely be used for screening prior to, and monitoring during, IPT.

PS-100951-13   Risky behaviour among PLHAS on HAART

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Background: Unprotected sex is several times riskier among PLWHAs on ART. Study objectives were to examine the prevalence of high risk behaviour among PLHAs, assess predictability of HIV re-infection. Assess access to sexual health information, HIV prevention and care programs in a sample of 18–40 year old PLWHAs on ART in Zambia.
Methods: 220 PLHAs completed questionnaires in which some answers were given orally and others in writing: Variables include HIV/AIDS knowledge, sexual behaviour, perceived risk, and knowledge on Partners ART regimen, risk reduction intentions, peer norms and partner risk levels.
Results: Unprotected Sex between PLWHAs is at the core of HIV re-infection in many Zambian contexts with consequences for drug resistance, treatment failure and subsequently transmitting the resistant strains of a virus to a partner who is not infected creating the risk of such partners developing primary drug resistance. 20% of female PLWHAs reported having multiple concurrent sexual partners. 18% reported having had syphilis but blamed medical practitioners for not screening them routinely for STI. Below 1% requested for an RPR test. 10% reported not being sexually active as a result of the information they were given when they were being initiated on HAART. 3% reported behaviour reduction intentions; 33% believe sex between PLWHAs is safe. 15% supported condom use; 68% reported unprotected sex in extra marital affairs. 55% reported having unprotected sex with both their wives and mistresses.
Conclusions: Wrong information shared in support

groups regarding having unprotected sex with a partner taking the same regimen is an impediment to condom use and fuels the high rise in risk behaviour making some assume that 'unprotected sex with a fellow PLWHA is safe'. Services should mount HIV prevention programs for PLHAs by introducing regular group counselling centred on behaviour change and safer sex and consequently reduce HIV incidence in Zambia.

PS-100970-13   Inequalities of gender an impediment to HIV prevention in Zambia

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Issues: In the HIV/AIDS era, gender: defined as the array of societal beliefs, norms, customs and practices that define 'masculine' and 'feminine' attributes and behaviors plays an integral role in determining an individual's vulnerability to infection, his or her ability to access care, support or treatment, and the ability to cope when infected or affected. Women in most African countries are cast as 'domestic reproductive agents' which expose them to HIV-TB co-infection and other sexually transmitted infections (STIs).

Description: In Zambia, women represent more than 60% of the total population, yet they are the most marginalized from political, governmental, nongovernmental through to social sectors. This background has continued to be a catalyst infernal fueling HIV infections among young and old women. A survey of AIDS service organizations still reinforce gender iniquities as most decision-making positions are in the hands of men. Women only account for less than 20% of leaders in decision making positions.

Lessons learned: Cultural behavior has spilled in to the NGO sector that seeks to overcome cultural practices that promote gender inequality. Men's cultural control of sex and matrimonial decisions suggests women's exposure to possible infection, unwanted pregnancies and HIV re-infection. Although 25% of women lead AIDS and human rights organizations, they still fall prey to gender inequality. Gender-based violence and denial, amplify fear of HIV serodisclosure to partners, which is critical to stopping HIV and ART implementation. In addition, customary law disadvantages women in the prevention of HIV/AIDS.

Recommendations: To adequately address gender inequality issues in the prevention of HIV, action is required in three areas: development of a supportive policy environment, strengthening health systems to make them more responsive to the specific needs of women and men, promotion of programmes that overcome obstacles to equitable access.

PS-101314-13   Community involvement is key in tuberculosis and HIV/AIDS care, treatment and adherence—TASO Jinja

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Introduction: The AIDS support organization (TASO) Jinja provides care to over 5000 people living with HIV (PLWHIV), 2300 of these are receiving antiretroviral therapy (ART). In the year 2009 TASO registered 65 smear positive TB cases. Over 80% completed treatment and were declared cured. This adherence is attributed to community involvement, a strategy that TASO developed to support clients.

Description: A model was developed in which a community with a number of TASO registered clients and is within a 75 km radius from the TASO service center was identified and the residents of these communities called upon to establish peer support groups, be part of the community ART/TB support agents, community nurses and volunteers. The role of these groups was to enhance adherence to HIV and TB treatment, address issues of stigma, family support to the patient and to promote HIV prevention. They also mobilize PLWHA for their drugs at either drug distribution points or outreach clinic sites, monitor drug adherence and make referrals appropriately. These volunteers are offered training by TASO in the basics of HIV/AIDS counseling and care prior to commencement of their duties. They are supervised and supported by TASO and the community leadership.

Lessons learnt: Communities are equipped with messages about TB-HIV treatment, adherence and prevention promoting retention of patients in care. Timely care for the bedridden clients by the home care team at their home. Less transport costs are incurred by PLWHA to seek services hence reduction missed drug refill appointments which promotes adherence. Regular refresher training for the community is required.

Recommendation: Involvement and strengthening capacity building at communities motivates and fosters the community to drive towards TB-HIV prevention and TB/ART adherence.

PS-101510-13   Delivering IPT for HIV/AIDS patients in a larger scale in Brazil: fostering partnerships

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Background: Based upon the preliminary results of the THRio (TB-HIV in Rio) operational research, carried out in 29 TB, HIV/AIDS clinics of basic health care units in Rio City, which demonstrated significant i) intensification of TB case findings, as well as ii) provision of treatment of latent cases, reducing time of TST provision and IPT delivery.
Objectives: To share the benefits of lessons learned by THRio with other high burden metropolitan areas in Brazil, contributing to delivering IPT, expanding TB prevention for HIV patients according to the Brazilian's MoH guidelines.
Methods: Phase 1: Perform in loco visits to priority areas designated by NTP, NAP, to discuss capacity building methods with TB and HIV/AIDS program managers. Generate situational analysis through existing (a) epidemiological data and (b) provision of TB chemoprophylaxis for HIV/AIDS patients. Phase 2: Provide tools for a 'permanent education' process for managers and health care workers. This process focuses on: operational management; logistics of inputs; use of existing means to discarding active TB; epidemiological surveillance; biosafety measures; comprehensive care; participation of civil society. This capacity building model aligns with permanent education strategy, promoted by the Unified Health System in Brazil, which consists in reviewing work process under diverse perspectives: holistic health, care provision, team work, management of human resources, and promotion of affected people participation in delivery. Encourage analysis and identification of strategies to consolidate 'health as citizens' right'.
Main results: Promote tutors (facilitators) to revise the work process in their own context, together with their work colleagues. Engage health care workers, health program managers and civil society members in increasing delivery of IPT. Generate a 'tools box' with specific technical support in routines, process, diagnostics, referral system, etc, enabling IPT extended delivery.

PS-100519-13   Provision of isoniazid preventive therapy for tuberculosis in Rio de Janeiro city, Brazil

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Setting: The number of countries reporting data on isoniazid preventive therapy (IPT) for HIV-infected patients to the WHO has increased in the last years. Although the number who were provided IPT increased, only 50 000 were started on IPT in 2008. Brazil does not have a national reporting system for IPT although its use has been recommended for specific risk groups for many years. We evaluated the provision of IPT using a municipal reporting system implemented in Rio de Janeiro in 2005, the same year that a comprehensive intervention to scale up IPT for HIV-infected patients (THRio) was initiated in the city.
Methods: IPT reporting forms were mandated by the Municipal Health Secretariat and submitted by all local health units. Data from forms were entered into an Access database. We analyzed categories of patients receiving IPT from January 2005 to December 2009 using Stata 9.
Results: During the study period, IPT use was reported for 5663 people; 2835 (50%) were male and 2724 (52%) were younger than 15 years (mean age 16 years). Among the reasons for starting IPT there were 3485 (61%) close contacts of a smear positive TB case, 1605 (28%) HIV-positive people (380 had a history of TB contact) and 573 (10%) people with other conditions. From 2005 to 2009 there was a 15% increase in the number of people given IPT: 8% for contacts, 29% for people living with HIV and 14% for other conditions.
Conclusions: Over the last 5 years, there has been a steady increase on the provision of IPT in Rio de Janeiro city. The largest increase was observed for HIV-positive people probably related to the efforts to promote IPT in this population.

PS-100694-13   Implementing a quality improvement programme in a TB diagnostic facility in semi rural Swaziland

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Aim: Describe a successful paradigm shift in documenting, ownership and implementing quality continuous improvement for TB-HIV at facility level in Swaziland.

Background: Failure to implement cost effective interventions like cotrimoxazole preventive therapy impact quality of life and mortality of TB-HIV patients. Based on analysis of routine data, we found cotrimoxazole was administered to <25% of TB-HIV patients in Piggs Peak hospital even after training nurses on co-management. To address this gap, we worked with the Ministry of Health to apply improvement methods in a semi rural facility in Swaziland.

Methods: We sensitised facility management about quality improvement (QI) and formed a multidisciplinary team. The team assessed patient flow, the care process and service data to analyse performance gaps and root causes. We provided onsite training, a job aid on cotrimoxazole dosages, and monthly support supervision to review team progress. Seven indicators on integrated TB-HIV services were collected by the team through review of patient records and recorded in a documentation journal. On a quarterly basis the QI team, with assistance from a coach, completed a synthesis form to interpret their results and plan new actions.

Results: Changes made by the team included arranging for cotrimoxazole to be supplied directly to the TB clinic; revision of the TB register and treatment cards to include a place to record cotrimoxazole provision; display of job aids; and display of quarterly indicator trends. There was a dramatic increase in the proportion of TB patients receiving cotrimoxazole from a baseline of 25% (57/228) to 92% within the first six months and to 99% (139/141) within the next three months. To sustain the improvements, QI meetings have been institutionalized so that the team meets and plans without our involvement.

Conclusion: MOH staff can be empowered through QI approaches to make rapid changes in TB care.

PS-101038-13   Community strengthening to link services, education and follow-up for improved TB outcomes

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Background: Namibia has one of the highest TB disease burdens in the world (765/100 000). TB treatment in the country is decentralized to the clinic level, and the necessary linkages between communities and these clinics are weak. Each clinic serves a catchment area of between 25–60 km, making logistics a major challenge for health service provision. This, in addition to a 60% TB-HIV co-infection rate, is contributing to the TB burden and poor treatment outcomes. In 2008, Project HOPE began mobilizing and rebuilding a cadre of community outreach workers to strengthen these linkages in the Oshana and Oshikoto Regions.

Intervention: Through community outreach efforts, intense data collection, and caseload mapping, Project HOPE has assisted the Ministry of Health and Social Services in strengthening case detection, monitoring and evaluation, and defaulter tracing. Weekly household visits are conducted by community volunteers, who reinforce adherence counseling, education, close contact referrals (including for IPT), HIV testing, and conduct in-depth interviews for defaulters.

Results: Among smear positive cases, cure rates recorded in quarter 4 in 2008 in Oshana and Oshikoto improved in 2009, from 59% to 62% and 74% to 77%, respectively. Treatment success rate in Oshikoto also increased from 81% to 92%. Defaulters within our 31 sites decreased from 23 to 9 in Oshana and 24 to 8 in Oshikoto, attributed to a near 100% tracing effort. Poor systematic recording around defaulters and treatment outcomes continues to be a major contributor to inaccurate and inconsistent data.

Conclusions and recommendations: Utilizing a community systems strengthening approach to TB prevention/management through reinforcement of linkages between communities and health facilities can be a highly sustainable strategy with real potential for national scale-up. Household level education to patients and family members with continuous follow-up visits is the crux for success in rural settings.

PS-101051-13   HEALTHQUAL: strengthening TB elimination through quality improvement in HIV clinics in Namibia

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Background: The HEALTHQUAL (HQ) quality management (QM) model utilizes performance measurement (PM) and QI strategies to build clinic level capacity for improving health care delivery. As part of their national HQ program (HQ-N), the Namibian Ministry of Health has developed an indicator to monitor clinic use of IPT to prevent TB among HIV-positive patients (PLHIV). QI interventions to strengthen local efforts to aggressively treat LTBI in the clinic setting have effectively advanced public health goals.

Methods: 16 participating clinics measured IPT enrollment among PLHIV not currently on TB treatment without documented contraindication. Clinic quality teams analyze processes of how IPT is delivered and then use their conclusions to direct specific intervention strategies aimed at increasing IPT. Of 12 QI projects, 8 utilized multi-component interventions.

Improvement strategies included use of patient passport stamps, IPT assessment forms and a dedicated IPT registry to improve documentation; improved patient education improved IPT accessibility through service co-location task-shifting; rescheduling visit times to combine activities and improved staff awareness of IPT's importance.

Results: Aggregated IPT indicator scores improved from 15% ($n = 1977$) to 20% ($n = 1646$) between baseline and follow-up measurements. 9 of 16 (56%) clinics improved scores by an average of 20% during this same period. PM data directed IPT QI projects at 9 clinics. 5 of the 5 clinics with comparable pre- and post-activity measures improved IPT scores by an average of 23%.

Conclusions: HQ-N's improvements in IPT enrollment among PLHIV suggest that country led QI activities strengthen the public health approach to TB elimination.

PS-101053-13 Implementing quality improvement in HIV clinics in four countries to strengthen TB diagnosis

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Background: The HEALTHQUAL quality management (QM) model utilizes performance data and QI strategies to intensify case detection and improve accurate diagnosis of TB. National QM programs in Uganda, Mozambique, Namibia, Nigeria and Guyana use TB clinical screen (TBCS) and TB diagnostic evaluation (TBDE) measures to direct QI interventions that systematize clinic processes to improve both clinical care and TB elimination.

Methods: Multidisciplinary teams identify factors affecting system-level performance and implement targeted QI strategies. Of 53 QI projects from all countries, 36 projects (68%) utilized multi-component interventions. Strategies most commonly implemented included development of specific screening forms and documentation changes (60%) training staff about the importance of TB screening (36%) and improved patient education/ counseling (25%).

Results: Each MOH-led program collected TBCS and TBDE data. 171 clinics extracted TBCS measures from 37 273 patient charts; 140 clinics extracted TBDE measures from 2262 charts. All 44 clinics with multiple rounds of TBCS data and 15/19 with TBDE data improved these scores, demonstrating average improvements of 33% ($n = 23\,459$) and 77% ($n = 1831$), respectively. 46 clinics have used these data to

direct 48 QI projects addressing TBSC and TBDE. Among the 19 TBCS and 11 TBDE QI projects with comparable pre-and post-intervention measures, 18 (95%) and 10 (91%) demonstrated average improvements of 42% and 46% respectively.

Conclusions: Consistent improvements in performance following focused QI interventions suggest that MOH-led QM activities strengthen the PH approach to TB elimination. QI programs should be considered a key component of PH elimination strategies and linked to TB data systems.

PS-101350-13 Pilot of a TB-HIV peer program in health centers in Lusaka, Zambia

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Background: With up to 70% of TB patients co-infected with HIV in Zambia, access to provider initiated testing and counseling (PITC) and enrollment in HIV care is a priority of the Zambian Ministry of Health. In Lusaka we documented suboptimal uptake of HIV counseling and testing (77%) and enrollment in HIV care (59%). In an attempt to improve this we implemented and evaluated a TB-HIV Peer model in health centers in Lusaka.

Methods: We piloted a six month TB-HIV Peer Educator program at two clinics in Lusaka from September 2008 to February 2009, with the goal of improving PITC and ART enrollment rates. Two volunteers per health centre were selected and trained to work with co-infected patients at both TB and ART clinics, provide extra post PITC counseling, referrals and escort patients for enrollment. We present the program results using data from two clinics up to February 2009. χ^2 tests were used to explore differences in enrollment in ART care for TB patients pre- to post-implementation.

Results: During the first six months of the program, the proportion of TB patients among all new ART enrollees in the two clinics went from 16 (12%) to 18 (13%), $P = 0.94$; and increased from 17 (10%) to 24 (14%), $P = 0.04$. In three comparison clinics, these proportions remained static or decreased from baseline to 6 months: from 13 (11%) to 6 (3%), $P < 0.05$; from 10 (6.6%) to 12 (7.3%), $P = 0.84$; and from 15 (12%) to 9 (6%), $P = 0.01$.

Conclusions: Preliminary data demonstrates that a peer driven model of referral and enrollment of HIV infected TB patients can increase enrollment in HIV care. Peer educator programs require further evaluation but appear to improve patient referral in settings with health care worker shortages.

PS-101400-13   Community volunteers involved in TB follow-up: TASO Masindi experience

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Background: TB is one of the most common opportunistic infection associated with HIV/AIDS infection. Prevention and control of TB infection posses challenges especially in regard to follow up of patients diagnosed with TB and are on treatment. Therefore strategies targeting adequate follow up of patients on treatment usually result in good TB treatment outcomes.

Response: The AIDS Support Organization (TASO) is a national non governmental organization in Uganda, involved in HIV prevention, care and support both at facility and community. TASO Masindi one of the 11 branches of the organization put up the following strategies to ensure follow up of patients on TB care. Community volunteers were trained on interpersonal communication to equip them with skills and knowledge to encourage their fellow community members to seek TB and HIV/AIDS care. They were also trained on detection of symptoms of TB and encouraged to refer suspected cases of TB for care and further support. Community volunteers were also encouraged to work with local leaders to educate communities about TB. The staff at the TASO centre carry out home visits to patients on TB treatment and also conduct support supervision of the community volunteers on a weekly basis to ensure quality of their work.

Lessons learnt: Most of the patients on TB treatment are followed up. Out of the 107 patients diagnosed with TB in 2009, 100% were followed up by the community volunteers, 18.7% cared for at home by the home care team, and 35.5% received psychosocial support through home visiting. There is complementary effort from both teams to follow up patients on TB treatment. There is reduction in stigma associated with TB disease in the communities.

Conclusion: Involvement of community volunteers in TB follow up if adopted yields good and practical result in TB management.

ADULT AND CHILD LUNG HEALTH

PS-100236-13   Perceived risk of getting Influenza A-H1N1 and behavioural responses among rural community, Malaysia

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Background: Influenza A (H1N1) pandemic is the most recent threat to Malaysians after the local media reported the first case in the country in May 2009.

Aim: To investigate the individuals perceived risk of getting infected with Influenza A (H1N1) and to recognize the behavioral responses regarding preventive and control practices among the rural community.

Methods: A cross-sectional study was conducted in the month of January 2010. A random sample of 660 adults attending four health clinics in the south part of Perak were interviewed by using well constructed questionnaires. The questionnaires were available in two languages (English and the national language). All respondents were aged 18 years and more. Data were analyzed using SPSS Version 16.

Results: The mean age of the respondents was 37.05 ± 15.02 years old. Respondents were predominately females (59.8%) compared to males (40.2%). Forty four percent of the respondent perceived as very high high risks of getting the infection, 13.8% perceived as moderate low risk and 42.2% no risk. Forty eight percentages of respondents will regularly isolate themselves when ill, 64.9% will regularly practice quarantine when instructed while 65.4% will follow instruction on temporary closure of schools/ working places.

Conclusion: This study provides a baseline data on individual risk perceptions and practices during pandemic which is important in order to identify further communication needs.

PS-100299-13   Epidemiological pattern of acute respiratory infection among under fives in Al Mazar, Al Janoub

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Aim: The aim of the present study was to conduct a cross sectional study to assess some of the epidemiological pattern of acute respiratory infection (ARI) among under fives in Al Mazar, Al Janouby district—south Jordan, also prevalence of ARI and its relation to body measurement.

Methods: All children under five years old who attend the Al Mazar, Al Janouby CPHCC in the selected three days per week for two successive months from 8 am to 2 pm were considered in this study, total number of children = 654 (324 males, 330 females) Mothers or relative were interviewed and direct personal contact utilized heavily, in additions to general physical examination with emphasize on the respiratory system, also weight, height and head circumference were measured.

Results: The prevalence of ARI was significantly increased with decrease age (OR = 2.1, $P = 0.048$). Overcrowding was significantly associated with increased prevalence of ARI (t = 6.25, $P < 0.001$). Breastfeeding protects children against ARI (OR = 2.1, $P = 0.048$). Bad ventilation of the houses was associated with more episodes of ARI (OR = 4.5, $P = 0.016$). Rearing of animals or bird was significant

(OR = 2.2, P = 0.005). Use of kerosene and wood in heating and cooking (OR = 10, P < 0.001).

Conclusion: Short succeeding inter-birth interval and overcrowding was significantly associated with increased prevalence of ARI. Breast feeding protects children against ARI. Bad ventilation of the houses was associated with more episodes of ARI.

Table   Personal characteristics of children with ARI

	Sample n	Prevalence of ARI %	Odds ratio	P value*
Age				
First year	197	17.8	2.10	0.048
Second year	148	14.9	1.69	0.189
Third year	132	10.6	1.15	0.748
Fourth year	107	9.3	1.00	0.013
Fifth year	70	22.9	2.87	0.003 (trend)
Family income JD/month				
<100	63	30.2	5.61	
100–199	175	22.9	3.85	
200–499	374	9.4	1.34	
500+	42	7.1	1.00	0.000 (trend)
Household size				
≤3 persons	92	10.9	1.00	
4–9 persons	524	13.9	1.33	
10+ persons	38	36.8	4.78	0.026 (trend)
Mother's educational level				
Illiterate	57	28.1	2.56	0.003
Primary, preparatory, secondary	423	13.2	1.00	0.714
Diploma, university	174	14.4	1.10	0.015 (trend)

PS-100923-13   Niveau de la pollution intérieure et extérieure à Cotonou : impact sur la santé respiratoire

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Objectif : Apprécier l'impact de la pollution intérieure sur la santé respiratoire des personnes résidant dans les maisons situées aux alentours des carrefours.

Méthodes : Etude descriptive et analytique de type transversale, allant du 5 février au 5 juillet 2006. Le monoxyde de carbone, le dioxyde de soufre, le dioxyde d'azote ont été mesurés à l'intérieur et à l'extérieur de 60 maisons situées au voisinage d'une voie à haut trafic et d'une voie à faible trafic pendant 8 heures. Une spirométrie a été réalisée à chaque enquêté.

Résultats : Le niveau du CO est plus élevé dans le haut trafic par rapport au bas trafic : intérieur des maisons (65 contre 43,2 ppm), extérieur des maisons (160 ppm contre 115 ppm). Le niveau du SO2 est plus élevé dans le haut trafic que dans le bas trafic: Intérieur des maisons (2,8 contre 0,49 ppm), extérieur des maisons (4,3 contre 0,83 ppm). La fréquence des symptômes respiratoires est de 78,3% pour le haut trafic contre 43,3%

pour le bas trafic (P = 0,000 ; OR 4,73 ; IC95% 2,13–10,51). La fréquence des anomalies spirométriques est de 23,3% pour le haut trafic contre 5% pour le bas trafic (P = 0,004 ; OR = 5,78 ; IC95% 1,43–27,10).

Conclusion : Le niveau de pollution est plus élevé à l'intérieur des maisons du haut trafic. Des troubles respiratoires à la fois fonctionnels et spirométriques ont été mis en évidence.

PS-100047-13   Body fat and asthma prevalence in children

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Introduction: Obesity is thought to increase the risk of asthma, especially in women. It increases the level of circulating IL6 and leptin which both down regulate regulatory T-lymphocytes (1).

Objectives: To compare the following:
   —Asthma prevalence of male and female children.
   —Body fat % in male and female children.
   —Body fat % in asthmatic and non asthmatic children.

Design and setting: This was a cross-sectional study performed in Kosti city 300 km south to Khartoum, the capital of Sudan. ISAAC questionnaire was distributed to 500 school children (250 males and 250 females) of 13–14 years of age. Body fat % using a sensitive body weight balance and skin fold caliber was determined for the asthmatics and a comparable randomly selected control of non asthmatics. Body fat % was compared between males and females, asthmatic and non asthmatics and then correlated to asthma prevalence. SPSS computer program was used for analysis.

Results: Asthma prevalence according to wheeze hearing was found to be 5.6% in male children and 7.2% in females. Body fat % in females was found to be 18.28% ± 5.10 in asthmatics and 16.01% ± 3.92 in non asthmatics (P = 0.08). Body fat % in males was found to be 16.67% ± 5.78 in asthmatics and 14.04% ± 3.44 in non asthmatics (P = 0.54).

Table   Body fat % in asthmatics and non asthmatics

	Asthmatics Mean % ± SD	Non asthmatics Mean % ± SD	P (P ≤ 0.05 for significance)
Males	16.67 ± 5.78	14.04 ± 3.44	0.54
Females	18.28 ± 5.10	16.01 ± 3.92	0.08

Conclusion: Both asthmatic males and females showed higher body fat % than non-asthmatics. Females showed higher asthma prevalence as well as

fat %. Although these results are below significance, but support other findings that increase in body fat is a risk factor for asthma.

1 Hersoug L G, Linneberg A. The link between epidemics of obesity and allergic diseases: does obesity induce decreased immune tolerance. Allergy 2007; 62: 1205–1213.

PS-100054-13   Genetic predisposition to asthma in Sudanese population

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Setting: In ISAAC phase 111 the prevalence of asthma in Sudanese children 13–14 years old was found to be 12.5% and in adult workers was 10%. Family history of asthma or allergies were reported by most of them. It is documented in previous studies in Caucasians that asthma has heritable linkage, with strong immune component in its pathogenesis, including IL-4, IL-5, IL-9 and IL-13, derived from T helper type2 cells.

Objectives: To detect if the polymorphisms of IL-9, IL-13, in chromosome 5 and IL-4R gene in chromosome16 is contributing to asthma in Sudanese population; to estimate total immunoglobulin E levels, and count with performing eosinophils skin prick test.

Methodology: 100 families were included, based on sample of nuclear and extended families. An interview questionnaire was filled for each individual of the family. Lung function and skin prick test were done. Blood sample for DNA analysis, immunoglobulin E, and eosinophil count were taken. DNA extracts and genotyping for IL-9, IL-13 and IL-4R, polymorphisms was done using PCR.

Initial result: The pedigree confirm the likely genetic cause for asthma, as shown in one extended family including more than 80 members, 54 of them are asthmatics. Level of total immunoglobulin E (80.8%) and eosinophil count (53.4%) was found to be high in asthmatics (73/145). Hypersensitivity symptoms to six allergens showed positive skin test ($P = 0.00$). Genotyping for IL-9, IL-13 and IL-4R in asthmatics was found to be 44.4%, 27.5% and 47%, for homozygous wild type, 87.5%, 60%, 53.3% for homozygous mutant type, and 47.6%, 75%, 75% for heterozygous type respectively.

Conclusion: Asthma seems to run in families in Sudan and show strong linkage to genes. High total serum IgE levels and high Eosinophil count have been found to be correlated with asthma. There is strong correlation between skin test, hypersensitivity symptoms and asthma. Mutant homozygosity and heterozygosity were observed in asthmatic patients.

PS-100088-13   Relation between perinatal life and contracting asthma by the child

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Background: Asthma is one of the most common important chronic diseases of children. It's prevalence has risen sharply over the past 40 years world wide. Reasons for this dramatic increase are not yet clear. It seems that as a result of package of changes in the intrauterine and infant environment.

Aims: To investigate the relationship between asthma occurrence and perinatal life to detect if perinatal life status acts as a risk factors for asthma.

Materials and methods: Cross-sectional study conducted in Baghdad (Capital of Iraq) on 2262 primary school children. A well constructed standardized questionnaire were completed by their parents. Questionnaire concentrated on the possible risk factors including type of delivery, birth weight, duration of breast feeding and cigarette smoking exposure.

Results: Children with history of prematurely were significantly having a higher rate (38.7%) of asthma ($\chi^2 = 3.96$), compared to those who born at full term (28.1%). Prematurity was a risk factor for having asthma (OR = 1.61). The association between type of delivery whether normal (28.6%) or cesarean section (27%) and asthma occurrence was not significant. History of LBW showed a significant higher rate (45.4%) of asthma than those with no such a history (25.7%). LBW acts as a significant risk factor for developing asthma (OR = 2.41). Children fed exclusive by breastfeeding (BF) demonstrated higher prevalence of asthma (29.2%) than those with no such history (26.4%). Duration of BF has no significant relation with development of asthma. A significantly higher prevalence of asthma among children with history of intrauterine exposure to cigarette smoking by their mothers (60.2%) or their father (39.1%) compared to the control group.

Conclusion and recommendation: Cigarette smoking, premature birth and LBW act as risk factors for asthma. Therefore good antenatal care and quitting smoking are highly recommended.

PS-100090-13   Does socio-economic status act as a risk factor for the development of asthma in children?

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Background: Asthma is one of the commonest chronic diseases of children.

Aims: To fill the gap in data concerning this disease in

Iraq, we investigated the sociodemographic and other life style related to asthma occurrence among primary school children.

Materials and methods: A cross-sectional study was conducted in Baghdad on 2262 primary school children aged 6–12 years, a well constructed standardized modified questionnaires of ISAAC were completed by the parents of the chosen children.

Results: Asthma prevalence was 28.5% it is higher (29.4%) in males than females (27.8%) this difference was not significant ($\chi^2 = 0.63$). However we detect that, being a male will be more exposed to risk of developing asthma (OR = 1.08, 95%CI = 0.9–1.3) compared to females. Our study detected that the prevalence of asthma is increasing steadily (27.4%), (28.3%) and (39.5%) with increased crowding rate (CR) (< 3, 5–5, >5) respectively. With significant association has been found between level of (CR) and asthma ($\chi^2 = 9.52$, $P = 0.009$). Interestingly by calculating OR for CR (3–5 vs. < 3) and (>5 vs. <3), we detect that only when the CR is > 5 acts as a significant risk factor for asthma occurrence (OR = 1.65, 95%CI = 1.1–2.4). Higher rate of asthma (29.2%) among those residing urban area compared to (25.2%), those in rural area morever those residing urban area were at marginal significant higher risk of exposure to asthma (OR = 1.23, 95%CI = 0.96–1.57).

Conclusion and recommendation: Efforts must be concentrated for hygienic environment in order to overcome this health problem.

PS-100186-13   A study of prevalence of asthma and associated risk factors in rural school children in South India

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Background: Childhood asthma is under-recognized, under-estimated and undertreated. Several studies in India have reported increasing prevalence of asthma among children. However, there is a paucity of information about prevalence of asthma among children in rural parts of India. This was the challenge addressed in this study.

Design/methods: This was a cross sectional study aimed at estimating prevalence of asthma among children in a rural area in India and identifying associated risk factors. Total enumeration of 588 children attending secondary schools in an area covered by a primary health center in a rural area in India was done by means of a locally modified version of the MRC (Medical Research Council) questionnaire.

Results: Prevalence of asthma by any of the three criteria (physician diagnosis, wheezing in the past one year or active inhaler use) was 4.9% (29/588) which

is higher than what was found in two studies in rural north India. Results of univariate and multivariate analysis of risk factors are shown in the Table.

Conclusions and recommendations: The results alert us about a relatively high prevalence of asthma among children in rural south India and prompt us to screen children for asthma under school health programs to enable early initiation of therapy. Focusing on those with risk factors may help increase the yield.

Table Univariate and multivariate analysis of risk factors for asthma

Risk factors*	Odds ratio	95%CI
Univariate analysis		
Male sex	2.99	1.19–7.45
Dusty house environment	5.14	2.21–11.95
History of known allergies since birth	4.05	1.70–9.64
Family history of asthma	2.54	1.12–5.77
Multivariate analysis	Adjusted odds ratio	
Male sex	2.19	1.13–7.47
Dusty house environment	3.54	1.37–9.12

* $P < 0.05$ for all risk factors shown.

PS-101086-13   Use of cell phone technology in asthma defaulters' tracing in Khartoum State, Sudan

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Setting: Asthma symptoms prevalence was found to be 12.5% in children and 10% in adults in Khartoum, Sudan. A pilot study on asthma management following the Union guidelines was established in 10 centers in Khartoum. Defaulter rates has increased dramaticaly recently.

Objectives: To assess the effect of using cell phone technology to trace asthma defaulters.

Method: A pilot study carried out in the period from 2009 to 2010. The exercise was performed in ten asthma referral centers at Khartoum state. All Patients seen at referred were asked to give their personal phone number. The numbers were written on asthma patients register cards. Any patient discontinued his follow up at the referral clinic is considered as a defaulter. 128 cases were selected randomly and phoned.

Results: 128 cases were included. 20% of cases defaulted from the first appointment and the rest from the subsequent ones. 98 out of 128 cases were reached by cell phone (76.6%) and 30 were not reachable (23.4%).The cost of single cell phone was 0.28 US Dollar. 30.6% of cases defaulted because of increased turnover of focal persons, 23.5% because they were improved, 18.4% due to unavailability of drugs, 9.2% were intermittent asthma from the start, 8.2%

travelled to other locations, 6.1% had looked for other medical advice and only 4% due to financial causes.

Conclusion:

1 Cell phone use is an effective and cheap means of tracing defaulters.
2 The involvement of more than one phone number, e.g., number of patient's relative or friend will improve the effect.
3 Intermittent asthma cases should be excluded from the start because they overestimate the number of defaulters.
4 Further study is needed to clarify the cause of high turnover of focal persons.

PS-100369-13   Availability of reduced-priced medications for bronchial asthma patients in Kyrgyz Republic

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Aim: To study the awareness of bronchial asthma patients along with medical professionals about the governmental reduced-priced medications opportunities in Kyrgyz Republic.

Methods: 100 bronchial asthma patients, 203 medical professionals from 25 medical institutions (capital and countryside) were subjected to specially designed questionnaires. Besides, 77 bronchial asthma out-patient management cards were reviewed along with Mandatory Health Insurance Fund (MHIF) database.

Results: 84% asthma patients in the study were aware of price discounts, 74% obtained reduced-priced prescriptions for beclamethasone, and only 52% patients purchased the medication in a pharmacy. Patients in countryside were more likely to be unaware of beclomethasone allowance (10.5%) compared to the capital (20%) ($P < 0.05$). 83.7% medicals in the study were aware of the list of diseases supported by preferential governmental programmes. We found primary level medicals to be more aware (95.5%) of price discounts for asthma patients compared to hospital medicals (84.4%) ($P < 0.05$). No differences were detected in awareness between capital and rural medicals. We also found low awareness of Family Medical Training Centres trainers.

Conclusion: In general, bronchial asthma patients along with family doctors in the country were aware of reduced priced medications offered by the government. However, low awareness of hospital doctors and Family Medical Training Centres trainers about the reduced-priced governmental allowances for bron-

chial asthma patients may emerge as one of the reasons of insufficient coordination between healthcare levels in managing bronchial asthma patients.

PS-100456-13   Relationship between paternal smoking and childhood asthma control

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Passive smoking is a well known factor of morbidity and mortality. It could cause or worsen many respiratory diseases. It increases the occurrence of asthma in children and exacerbates its symptoms. Few studies investigated paternal smoking and children's asthma severity. The aim of our study is to evaluate the relationship between father's smoking degree and control of childhood asthma. Fifty eight children aged less than 16 years, followed in our consultation for asthma from 2001 to 2010 were prospectively included. All children were exposed to paternal passive smoking. Children exposed to both mother and father's smoking were excluded. Asthma control was evaluated based on GINA criteria. Children were 37 boys and 21 girls. The average age was 8.8 years (2–16). Mean passive smoking was evaluated to 27 package/year (PY). Forty two children were exposed in utero to passive paternal smoking (72.4%), 26 had atopic asthma (44.8%) and 23 had a past history of bronchiolitis (39.6%). The main symptom was chronic cough (50 children had chronic cough and 43 had wheezing). Forty two children had allergic rhinitis (72.4%). Asthma was uncontrolled in 38%. The number of exacerbation per year was 4 times high for patients with a passive smoking at more than 20 PY compared to those at less than 20 PY (16 vs. 4, $P < 0.05$). In addition, exacerbation number was correlated to paternal smoking's duration. We conclude that asthma control is correlated to paternal smoking degree and duration. For a better control and management of asthma in children, parents should be educated and informed of their risky smoking behavior.

PS-101384-13   Is self management by systemic corticosteroid therapy in asthma an up-to-date problem?

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Introduction: The aim of asthma therapy is to achieve and maintain disease control. Clinicians' behavior is crucial in terms of prescribing the best possible treatment, carrying out appropriate follow-up and ensuring adherence to treatment with minimal side effects. The benefits of inhaled corticosteroids are largely proved reducing systemic steroids administrations.

Although systemic corticosteroids are rarely prescribed, some patients continue to self manage their disease with these.

Aim: To investigate influence of systemic steroids on asthma management and to study main side effects.

Methods: Our study is retrospective study based on files of asthmatic patients hospitalized in our respiratory unit from January 2002 at December 2008. The patients who were included are those taking a systemic corticosteroid therapy at least once a month during in the last year.

Results: 10 patients from 177 studied were included (5%). 5 men and 5 women. The mean age of the patients is 53 years. 1 patient on 2 was irregularly followed up. The average BMI is 30.The asthma is classified mild intermittent in 10%, mild persistent in 10% and severe persistent asthma in 80%. The most frequent complication is diabetes (50%). The mean period of hospitalization is 14 days while it is 11 days for the patients without self management.

Conclusion: Despite the availability of effective asthma treatments and evidence-based management guidelines focusing on asthma control, many patients have asthma that is inadequately controlled because of abuse steroid use.Our findings provide one possible explanation of why asthma control levels are currently unsatisfactory in real life.

BACTERIOLOGY AND IMMUNOLOGY

PS-100066-13   *Mycobacterium bovis* in Tunisia: location and resistance profile of antibiotics

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Bovine tuberculosis, caused by *Mycobacterium bovis* is a zoonotic infection that also affects humans. The consumption of unpasteurized milk or dairy products as well as close contact with the infected animals plays a major role in the spread of the disease. In this study, we report 22 cases of human tuberculosis where *M. bovis* was isolated. Most of the clinical samples were obtained from lymph nodes ($n = 18$). Other samples were 2 sputum, one mammary tumefaction and one cutaneous suppuration. The age of the patients varies from 5 to 47 years. Acid-fast bacilli identification was negative at the majority of cases. The culture on Löwenstein-Jensen medium allowed isolating *M. bovis* within 42 to 60 days. The biochemical identification was confirmed by a molecular method (GenoType MTBC. Hain LifeScience). 20 strains were susceptible to antituberculous drugs. Two strains isolated from chronic lymphadenopathy were resistant, one was monoresistant to rifampicine and another was multidrug resistant (SHRE). The incidence of bo-

vine tuberculosis is not well evaluated in Tunisia. Epidemiological and public health aspects should be analyzed to control the disease in humans and animals.

PS-101471-13   Risk factors associated with rifampicin resistance in *Mycobacterium tuberculosis* complex strains

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Objective: To investigate risk factors associated to rifampicin (RMP) resistance in *M. tuberculosis* complex strains in TB patients treated previously.

Methods: Fifty-four TB patients treated previously (failures of first and second cures, relapses, and abandonments), were included in the study. They were interviewed, examining the parameters investigated: regular intake of alcohol and use of traditional treatment; gastric disorders and HIV serological status. Sputum was sown on solid medium Löwenstein-Jensen. *M. tuberculosis* resistance to isoniazid, rifampicin, streptomycin and ethambutol was determined using the proportion method. Patients were tested for HIV. Association between parameters explored and strain resistance to rifampicin were evaluated by odds ratio (OR) and 95% confidence intervals (95%CI).

Results: The mean age of the 54 patients was 37.9 ± 11.8 years [range 20–76 years]; 38 (70.4%) were male. All the patients were infected by *M. tuberculosis* and the multidrug resistance (MDR) rate was 44.4%. Ten (25.6%) patients among 39 tested for HIV were positive. Resistance to rifampicin was found in 8 (36.4%) among the 22 patients who used traditional treatment (OR = 1.25, 95%CI 0.40–3.9). Twenty-two (40.7%) drank alcohol regularly and 11 (50%) of them were resistant to rifampicin (OR = 1.9; 95%CI 0.6–5.7). Among 18 (33.3%) patients reported suffering from gastric problems, 13 (72.2%) were infected with *M. tuberculosis* strains resistant to rifampicin, (OR = 5, 9, 95%CI 1.6–20.6). The HIV status was not associated with resistance to this drug (OR = 1.23, 95%CI 0.29–5.19). A significant correlation was found between gastric disorders and resistance to rifampicin.

Conclusion: These results sustain the establishment of a dietary advice and especially the monitoring of gastric disorders in patients submitted to treatment including rifampicin, to prevent treatment failures.

PS-100082-13   Microevolution of *Mycobacterium tuberculosis* in Taiwan

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The distribution of *Mycobacterium tuberculosis* was reported had genotype relationship to geographic,

ethnicity, and population migration. A multi-center, three year collection of patient with 516 tubcerculosis isolates in Taiwan was conducted to demonstrated the microevolution in Taiwan: 1) 254 isolates from north Taiwan which had 58% of veterans, origin from Han Chinese migrated from China 60 years ago; 2) 38 patients with isolates came from hospital in mid-west coast, which located in central area of traffic line and had mix population of Taiwanese and aborigines in central mountain who migrated from south island China 4000–10000 years ago; 3) 211 isolates collected from south Taiwan which represented Taiwanese who migrated from China 200–400 years ago; and 4) 13 isolates from east coast of Taiwan, had aborigines Amis migrated from Phillippines 4000 to 10000 years ago. The isolates were genotyped with spoligotyping and standardized 12-loci-MIRU-VNTR typing. In general, Beijing and Beijing like family were major strains of tuberculosis spread in Taiwan in either in north (58%), east (53%), or south Taiwan (33%). The second common spoligotyping was Manilla strain (20%) in south Taiwan, and Haarlem strain in mid-west (18.4%) or east coast Taiwan (23%). International comparison by MIRU-VNTR phylogeny method toward Beijing Beijing like family indicated the north Taiwan lineage are similar to the strains isolated from other countries including Asia and Europe, and this relationship presented both in Taiwanese and veterans. Both north and south Taiwan MIRU lineage had high Hunter-Gaston discriminatory index, it means both lineage had independent evolution and community transmission environment, and had no evidence that derived from each other. Close contact still the main transmission pathway and local distribution within regions with microevolution relationship were represented in this study.
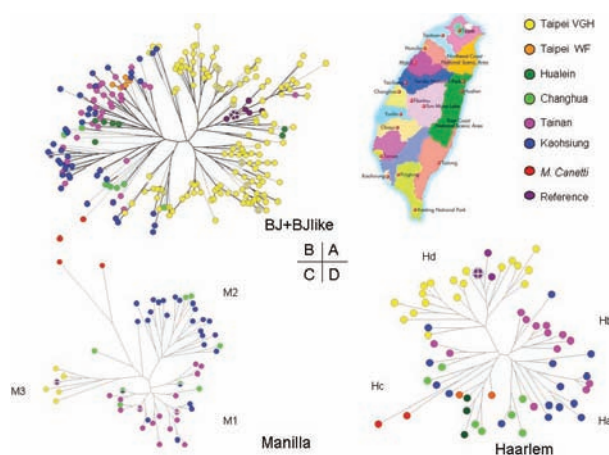
PS-100326-13   Risk of MDR-TB development in isoniazid-resistant TB cases

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Background: In Georgian National Center for Tuberculosis and Lung Diseases (NCTLD) treatment of isoniazid-resistant mono and poly DR-TB cases are performed according the international standards, despite of this rate of development MDR-TB is still high.
Aim: To determine the risk of acquisition of rifampicin-resistance in isoniazid-resistant TB cases in order to prevent development of MDR-TB cases.
Methods: With support of the United States Civilian Research Development Foundation (CRDF) grant (GEX1-002711-TB-06) resistance status of TB patients from NCTLD were collected since 2006. Statistical analysis of data was performed using Epi Info version 3.5.1.
Results: Of 605 patients 114 (18.8%) were DS-TB and 491 (81.2%) were DR-TB. From 197 (32.6%) mono and poly DR-TB cases isoniazid-resistance were found in 76 (12.6%) cases and rifampicin-resistance in 12 (1.98%) cases. From DS-TB cases MDR-TB is developed in 9 (8%) patients, from isoniazid-resistant DR-TB cases in 11 (14.5%) patients and from rifampicin-resistant DR-TB cases in 1 (8.3%) patient.
Conclusion: Findings confirm that the risk of development MDR-TB in isoniazid-resistant cases is higher compared to rifampicin-resistant and sensitive TB cases. Implementation of special measures for preventing MDR-TB is necessary. For example, the treatment of pulmonary TB cases with intensive regimen containing 6 months of rifampicin (2HRZE/4HR) should be recommended.

PS-100331-13   Treatment outcomes of MDR-TB cases

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Background: Standard treatment of MDR-TB was not available in framework of Georgian National TB Program until 2008 and drug resistance TB cases were treated by the first line TB drugs. It was important to obtain MDR-TB treatment outcomes data before of starting standard treatment and to compare this data with treatment outcomes after implementation of DOTS+ strategy.
Aim: To determine frequencies of treatment outcomes in new and previously treated MDR-TB cases.
Methods: Before implementation of DOTS+ strategy (2006–2008) from 605 TB patients the data of treat-

ment outcomes was collected. Statistical analyses of data was performed using Epi Info version 3.5.1.

Results: Study gave us ability to compare rates of different outcomes in drug susceptible (DS-TB) and MDR-TB cases. Highest rate of cured patients were observed in new DS-TB cases (56, 76.7%); highest rate of 'failure' were observed in new and re-treatment MDR-TB cases (17, 33.3% and 62, 29.5%). Warning was high rate of 'default' in all cases, especially in re-treatment DS-TB cases (16, 39.0%) and high rates of 'death', especially in re-treatment MDR-TB cases (70, 33.3%) (see Table).

Treatment outcomes	DS-TB (new) $n = 73$	MDR-TB (new) $n = 51$	DS-TB (re-treatment) $n = 41$	MDR-TB (re-treatment) $n = 210$
Cured	56 (76.7%)	9 (17.6%)	9 (22.0%)	21 (10.0%)
Completed	7 (9.6%)	6 (11.8%)	9 (22.0%)	22 (10.5%)
Default	5 (6.8%)	8 (15.7%)	16 (39.0%)	35 (16.7%)
Failure	1 (1.4%)	17 (33.3%)	0 (0%)	62 (29.5%)
Death	4 (5.8%)	11 (21.6%)	7 (17.0%)	70 (33.3%)

Conclusion: The highest rate of 'failure' and 'death' in MDR-TB cases, which were treated by first line TB drugs, confirms the necessity of DOTS+ strategy, but on the other hand we need confirmation that treatment with II line TB drugs will be able to reduce unsuccessful outcomes. Our study will continue in future and we wait to get interesting results by comparison of treatment outcomes data before and after standard treatment for MDR-TB.

PS-100376-13 Morphological changes in resection materials from phthisiosurgical patients with resistant pulmonary tuberculosis

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Target: To conduct the comparative analysis of morphological changes through resection materials investigation at fibrocavernous pulmonary tuberculosis (FPTB) in 95 patients with multi- and poly-drug resistance.

Objectives: To analyze the microscopic changes at FPTB in patients with MDR and in patients with poly-drug resistance by histological preparations.

Materials: Resection materials obtained in 75 patients with MDR-TB and in 20 patients with poly-drug resistant TB after pulmonectomy and lobectomy.

Results: Comparative analysis of morphological changes in patients with FPTB with MDR and poly-drug resistance revealed the general changes: active and progressing TB process course. The differentiating traits of the morphological changes of FPTB in patients with poly-drug resistance were as follows:
1) keeping of wide caseous necrotic layer in a cavity;
2) expressed infiltration of caseous masses with leukocytes with followed their dissolution due to proteolytic

enzymes from decomposing polymorphic nucleus leukocytes; 3) non-correspondence of the thickness of granulation layer with regard to the caseous necrotic layer with small number of epithelioid and single giant cells of Langhans; 4) thinness of the external fibrous layer, probably due to its expressed infiltration with lymphocytes, plasmatic cells and polymorphic nucleus leukocytes; 5) injury of bronchi with TB process and development of TB bronchitis.

PS-100483-13 Evaluation du traitement antituberculeux des patients co-infectés TB-VIH à Conakry

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L'objectif était d'évaluer les résultats du traitement antituberculeux chez les patients co-infectés TB-VIH en pneumo-phtisiologie. Pour la réalisation de ce travail, nous avons utilisé le registre de la tuberculose, les dossiers individuels des malades et une fiche d'enquête individuelle. Il s'agit d'une étude rétrospective de type descriptif de deux ans allant du 1ère Janvier 2005 au 31 Décembre 2006 qui a porté sur l'ensemble des malades hospitalisés dans le service de pneumo-phtisiologie de Conakry. Nous avons inclus, tous les dossiers des patients séropositifs pour le VIH présentant une tuberculose et hospitalisés dans le service. Ont été exclus, les dossiers incomplets. Nous avons enregistré 331 cas de co-infection TB/VIH sur un effectif de 1436 patients hospitalisés, soit 23,05%. La majorité des patients réside à Conakry (89%). Nous avons observé 218 cas (65,86%) de tuberculose pulmonaire dont 189 (57,1) à microscopie positive et 29 cas (8,8%) à microscopie négative et 113 cas de tuberculose extra pulmonaire soit 34,1%. Les cas de tuberculose pulmonaire à microscopie positive comprenaient 165 nouveaux cas et 24 cas de retraitement dont 21 rechutes, 2 cas d'échec et un cas de reprise après abandon de traitement. Dans les formes extra pulmonaires, la tuberculose des séreuses a été la plus fréquente (54,38%) suivie de la miliaire (36,05%) et de la tuberculose ganglionnaire (7,07%) 20/311 patients ont bénéficié du traitement ARV. Le taux de succès a été de 43% chez les nouveaux cas à frottis positifs celui de décès de 32,9%. Dans les tuberculoses à microscopie négative et les extra pulmonaires, les taux de traitement terminé ont été de 42,9% et de 45% et les taux de décès de 32,1% et 36,7% respectivement.

PS-100586-13   Toxicity of pulmonary tuberculosis first-line drugs

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Tuberculosis (TB), whatever is its localization, is an infectious disease which can be totally cured by combining antituberculous drugs. However, anti TB drugs could be associated to a high rate of adverse effects (AE) that can lead to therapeutic failure. The aim of our study is to determine the frequency and manifestations of AE associated with recommended first-line anti-TB drugs. Forty immuno-competent male patients with primary TB who initially received anti-TB therapy were evaluated retrospectively. AE and the timing of their occurrence, as well as subsequent modifications in the treatment regimen, were studied. The mean age was 38.24 years (range 17–75). The frequency of minor side effects was 77.7% and that of major side effects was 22.5%. The most commons were cutaneous reactions (40%) and hyper uricemia (40%). Hepatic toxicity was noticed in 20% of cases with a severe increase of hepatic enzyme levels in 2.5% of cases. Gastrointestinal intolerance occurred in 7.5% of cases. Haematological toxicity was noticed in 3 cases and ocular side effect in one case. AE were more common in the two first months of treatment (91.8%). Modification of the treatment regimen was necessary in 6 cases. Drug-induced hepatitis was the most adverse effect needing regimen change. Minor side effects of anti-TB drugs are common, including cutaneous reactions, gastrointestinal intolerance, haematological reactions and hepatitis. These AE must be recognised early, to reduce associated morbidity and mortality. Serious AE are rare and patients should be followed up by close monitoring for side effects related to anti-TB drugs.

PS-100624-13   Genetic analysis of multidrug-resistant *Mycobacterium tuberculosis* isolates in Kazakhstan

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Kazakhstan included in 14 countries with high rate of MDR-TB morbidity in European region WHO. The aim of our study was to characterize mutations associated with drug resistance to the rifampicin and isoniazid in *Mycobacterium tuberculosis* isolates from Kazakhstan. *M. tuberculosis* strains were isolated from TB patients in different regions of Kazakhstan. Drug susceptibility test was determined on Löwenstein-Jensen medium by absolute concentration method according WHO recommendations. Sequencing analysis of *rpo*B rifampicin resistance-determining region (RRDR) and of *kat*G gene, *oxy*R-*ahp*C intergenic region and *inh*A promoter region in 259 multidrug-resistant *M. tuberculosis* isolates were performed. The mutational analysis revealed the most frequent mutations associated with rifampicin and isoniazid resistance in mycobacteria are the substitutions at codons 531 (82.23%) and 315 (98.43%) in the *rpo*B and *kat*G genes, respectively. Also, we have found mutations with lower frequency at 526 (8.49%), 533 (1.54%) and 516 (1.15%) codons in *rpo*B gene. In 6.56% of the isolates no mutations in *rpo*B gene were found. These findings provide useful data on the mutation types of multidrug-resistant genes in *M. tuberculosis* isolates from Kazakhstan.

PS-100833-13   Assessment of laboratory practices that may contribute to low TB case detection in Ethiopia

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Background: High quality DOTS is dependent on efficient sputum smear microscopy. Ethiopia has a low TB case detection rate, with only 28% of smear positive TB patients detected (WHO estimates for 2007). USAID's Tuberculosis Control Assistance Program (TBCAP) is providing support in Ethiopia for TB control activities including laboratory strengthening. **Methodology:** Two rounds of baseline situation analysis to determine laboratory factors that may contribute to low TB case detection were conducted, in order to institute appropriate interventions. A structured questionnaire was used in six TBCAP supported zones. The first round included 3 zones of East Shoa, North Shoa and Gurage from July 2008 and the second round in January 2010 for Arsi, West Arsi, West Shoa and Awi zones. **Results:** Analysis of the questionnaire showed that most of the laboratory staff had received AFB microscopy training in 100% ($n = 8$) and 80% ($n = 10$) of laboratories in rounds 1 and 2 assessments respectively. Despite the training, laboratory practices were not uniformly standardized. Supportive supervision was not being implemented in all round 1 and in 80% of round 2 labs. SOPs were not in laboratories at baseline and only 50% and 10% of laboratories respectively performed quality control. Slide rechecking was done in 2/8 and 6/10 labs and feedback was received within 2 weeks in 1/8 and 2/10 labs respectively. After instituting focused lab interventions; providing training, SOPs, slides recheck and regular supervision with timely feedback, slide positivity in laboratories improved. These and other interventions increased the TB CDR from 30% to 64% over 8 months. **Conclusion:** TB case detection in laboratories can be improved by strengthening routine laboratory

activities. Training of staff is effective when it is followed-up with supportive supervision. TB laboratory strengthening plans should be informed by realistic gaps identified during situational analysis.

PS-100857-13   The role of sigma factors in the progression from rifampicin mono-resistance to MDR-TB

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Background: Rifampicin resistance occurs as a result of mutations in *rpo*B, which encodes the β subunit of DNA-dependant RNA polymerase in *Mycobacterium tuberculosis* The majority of rifampicin resistance worldwide can be attributed to mutations at codons 531, 526 and 516 of RpoB. Rifampicin mono-resistance is rarely seen, and usually occurs together with isoniazid resistance, which is defined as MDR-TB. Since in vitro mutation of sigma factors affects their binding affinity for the core RNA polymerase, it may be that mutations within *rpo*B result in preferential binding of alternative sigma factors, and through differential gene expression may result in isoniazid resistance.

Methods: Rifampicin-resistant *M. tuberculosis* H37Rv mutants were selected following growth in the presence of rifampicin. To determine the expression levels of genes encoding putative *M. tuberculosis* sigma factors, real-time reverse transcriptase-PCR was carried out using RNA from *M. tuberculosis* H37Rv RpoB mutants.

Results: The rifampicin-resistant *M. tuberculosis* H37Rv mutants obtained included isolates with RpoB S531L, S531W, S522L, H526D or H526Y mutations. The expression levels of the primary sigma factors sigA and sigB were equivalent in all mutants as compared to *M. tuberculosis* H37Rv, whilst sigI, sigL and sigM levels were not detectable in any of the strains. The level of expression of sigE in mutants carrying RpoB S531L, S531W and S522L was increased 3.8 to 7.2 fold relative to *M. tuberculosis* H37Rv.

Conclusions: Interestingly, SigE regulates fabD and acpM expression, two genes involved in the mycolic acid synthesis pathway, which is inhibited by isoniazid. The increased expression of sigE in RpoB mutants S531L/W and S522L may reflect increased binding affinity of SigE to RpoB, and thereby overexpression of fabD and acpM, resulting in isoniazid resistance.

PS-101064-13   Use of the GenoType® MTBDRplus assay to assess anti-TB drug resistance levels and patterns

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Background: Drug resistance levels and patterns among *Mycobacterium tuberculosis* isolates from newly diagnosed and previously treated tuberculosis patients in Mbarara, Uganda were investigated.

Methods: We enrolled, consecutively; all newly diagnosed and previously treated smear-positive TB patients aged ≥8 years. Isolates were tested for drug resistance against rifampicin and isoniazid using the Genotype® MDR-TBplus assay. HIV-1 testing was performed using two rapid HIV tests.

Results: A total of 125 isolates from 167 TB suspects 60% males with a mean age 33.7 years and HIV prevalence of 67.9% were analysed. 92.8% were new cases and 17.2% were retreatment cases. Resistance mutations to either RMP or INH were detected in 6.4% of the isolates. MDR, INH and RMP monoresistance was 3.2%, 4% and 5.6%, respectively. *rpo*B gene mutations were D516V, S531L, H526Y and H526D together with D516V, while one strain had a △1 mutation in the wild type probes. There were three strains with *kat*G (codon 315) gene mutations only and one strain with *inh*A gene mutation.

Table   Mutations associated with RIF and INH resistance in the eight resistant isolates

Study number	RMP resistance pattern (*rpo*β gene)		Isoniazid resistance pattern				
	WT probes	Mutant probes	*Kat*G probes		*inh*A probes		
			WT	Mutant	WT1	WT2	Mutant
08	—	D516V, H526Y, H526D	WT	—	wt	WT	C15T
29	—	D516V	WT	—	WT	WT	–
47	—	D516V	WT	—	WT	WT	–
102	—	—	wt	S315T1	WT	WT	–
291	△8	S531L	wt	S315T1	WT	WT	–
246	—	—	wt	S315T2	WT	WT	–
248	△1	—	WT	—	WT	WT	–
437	—	S531L	WT	—	WT	WT	–

Conclusion: TB resistance rate in Mbarara is relatively low with a substantial proportion of INH mono-resistance. GenoType® MTBDRplus assay can be used for rapid screening of MDR-TB in this setting.

PS-101205-13 Monitoring anti-tuberculosis drug induced chemical changes in *M. tuberculosis* by SERS

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Aim: To monitor antibiotic-induced chemical changes of *Mycobacterium tuberculosis* by surface-enhanced Raman spectroscopy (SERS) and to demonstrate the feasibility of using such a high-speed nondestructive optical technique for detecting the differences between drug-susceptible and drug-resistant strains.

Methods: Substrates with extremely large and uniform enhancing power are exploited for measuring the vibrational spectra of molecules on the cell-wall of *M. tuberculosis* by SERS. Thanks to the sensitivity of the method, the spectrum of single or few bacteria can be recorded in a few seconds, allowing real time monitoring of chemical changes on bacteria after being exposed to antibiotics. Based on the characteristic differences in the changes, drug susceptibility of *M. tuberculosis* can be identified. Pan-susceptible and mono-drug (isoniazid, rifampicin, ethambutol, or pyrazinamide) resistant *M. tuberculosis* were analyzed.

Results: The SERS spectra of a pan-susceptible *M. tuberculosis* strain exhibits dramatic changes in a few tens of minute after treating with isoniazid (INH), as shown in the following example (Figure). In contrast, the SERS spectra of an INH-resistant strain show relatively minor and stable changes. Two robust peaks (400 cm-1 and 525 cm-1) for INH resistant, while one (725 cm-1) for INH susceptible *M. tuberculosis* were identified.
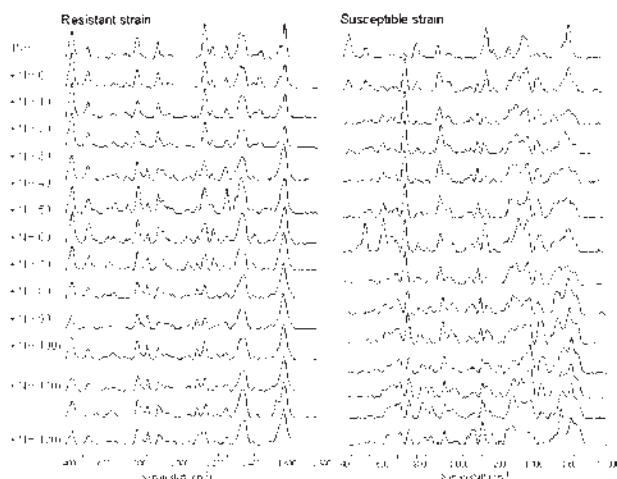
Conclusion: The SERS-based detection platform with single bacterium sensitivity opens unprecedented op-portunies for drug susceptibility testing of *M. tuberculosis* and assessing the efficacy of new drugs for tuberculosis.

PS-101291-13 SELDI-TOF-MS for detecting serum protein biomarkers of smoking in North Chinese Han males

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Objectives: To discover the potential biomarkers and establish a diagnostic pattern for smoking by using proteomic technology.

Methods: Serum proteomic spectra were generated by surface-enhanced laser desorption ionization time of flight mass spectrometry (SELDI-TOF-MS). A set of spectra, derived from analyzing serum from 40 smokers and 40 age- and sex-matched healthy non-smokers, was used to develop a decision tree model with a machine learning algorithm called decision boosting. A blinded testing set, including 10 smokers and 10 healthy non-smokers, was used to determine the accuracy of the model.

Results: The diagnostic pattern with a panel of three potential protein biomarkers of mass-to-charge (m/z) 3159.13, 7561.03, 9407.32 could accurately recognize 38 of 40 smokers and 39 of 40 non-smokers. Validation on the blinded testing set indicated that the decision tree could differentiate 8 of 10 smokers and 10 of 10 non-smokers.

Conclusions: The preliminary data suggested a potential application of SELDI-TOF-MS as an effective technology to profile serum proteome of smoking, and with pattern analysis, a diagnostic model comprising three potential biomarkers was indicated to differentiate smokers and non-smokers rapidly and precisely.

PS-101364-13 Efficiency of Plasmacluster ion in killing of *Mycobacterium tuberculosis* on culture media

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Setting: Prevention of tuberculosis transmission in environment is control ventilation, ultraviolet germicidal irradiation and filtration air with high efficiency particulate air filter. New innovation of Plasmacluster ion generation for air cleaning has been proved to be effective in killing pathogenic viruses, clinically important bacteria and fungus. There was no any study done for *Mycobacterium tuberculosis*.

Objective: To study the efficiency and exposure time of Plasmacluster ions in killing standard strain of

M. tuberculosis (H37Rv) and 50 isolated *M. tuberculosis* strains from tuberculosis patients on culture media in laboratory.

Method: Prepare suspension of bacteria with McFarland No.1 and diluted to 1:10000. Inoculate 0.1 ml. suspension on Middlebook 7H10 media for 5 media. Incubate media in incubator at 37°C for 48 hours to check contamination. Expose 4 media at a distance of 1 foot from Plasmaclustrer Ions Generator in a closed chamber. After 15, 30, 45 and 60 minutes brought out one media each time. The unexposed media was used as a control. Incubate all media in incubator and read result after 3 weeks. Standard strain was repeated test for 3 times.

Result: For standard strains of *M. tuberculosis* there was no growth after exposure time of 30 minutes. For clinical isolate strains, there was no growth after exposure time of 15, 30, 45 and 60 minutes in 4 (8%), 4 (8%), 9 (18%) and 19 (38%) strains respectively. In 14 (28%) strains which has growth on media after 60 minutes of exposure, the number of colony on media was declined according to the longer exposure time.

Conclusion: Plasmacluster ions can kill *M. tuberculosis*.

PS-101427-13   Financing of TB in a low-income country: the case of DRC

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Introduction: The TB Program has a Development Plan 2006-2015, which cost $545 861 560. Since 1996, the NTP applies the DOTS. The detection rate remains low (61%), but the success rate in treatment of new cases TPM + is 85% in 2005. The NTP is supported by the Government, the Global Fund (in Rounds 2, 5 and 6), Action Damien TLMI, USAID, The Union, WHO, ALM, UBS, CE detection rate is increasing with increased funding.

Objective: To show how PNTLT DRC could achieve efficient outcomes (indicators WHO) with a diversity of donors and the mode of financing.

Methodology: Full analysis of how and financing strategies of the Strategic Plan NTP DRC from 2006 to 2009.

Results: Four years after the implementation of its Strategic Plan, the NTP has mobilized $79 079 743 (14.49%). The Gap cover is $466 781 820 (85.51%) until 2015.

Conclusion: End 2009, the Strategic Plan has been funded at 14.49% and the number of diagnosed patients has increased from 98 139 to 111 851 for the same period.

PS-101444-13   Recruiting adolescents for an epidemiology study in Uganda in preparation for TB vaccine trials

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Background: A number of novel TB vaccines currently in early phases of development will need to be tested in large phase III trials in developing countries. Adolescents, a potential target population are not a usual target for vaccines and require both proxy consent and assent to participate. As a prerequisite, it is important to determine the incidence of TB and feasibility of forming, tracking and retaining a cohort in this population. As part of site preparation, we are conducting an epidemiological study to estimate the incidence and prevalence of Tuberculosis disease among adolescents in the Iganga/Mayuge Demographic Surveillance Site in Uganda.

Methods: A cohort of 7000 adolescents aged 12–18 years is being recruited and followed for two years. Adolescents identified from the DSS database are visited at home to obtain parental consent while assent is obtained at school. At enrolment, key demographic parameters, vital signs and relevant medical history are collected. All participants have TST administered to determine annual risk of TB infection. Participants identified as TB suspects as defined by the protocol undergo TB diagnostic work up which includes sputum coaching and collection of 2 sputum samples.

Results: Difficulty in obtaining parental consent and adjusting to the school calendar and schedule are the main challenges in recruitment. Out of 1269 participants enrolled, 1179 (93%) are school going. A total 499 met the criteria for TB diagnostic work up; 224 were TST positive ($\geqslant$10 mm), 69 had cough of $\geqslant$14 days and 106 had positive household contacts. So far, there are 6 smear positive participants of whom 4 are culture confirmed *M. tuberculosis* but none have HIV.

Conclusion: Early results indicate there is TB in this population and recruitment is feasible however sites need to devise ways of addressing the challenges.

PS-100778-13   The nutritional status IFN-γ response of household and non-household tuberculosis contacts

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Background: Malnutrition has long been associated with the development of tuberculosis and may be re-

sponsible for the premature deaths of individuals with active disease. Numerous studies have reported the usefulness of interferon gamma assay QuantiFERON Gold In-Tube assay (QFT) in diagnosing latent infection in close contacts of TB patients. Individuals in close contact with TB cases are considered to be a high risk group; however an adequate nutritional status may delay the progression to active disease. The aim of this study was to determine if a relationship exists between nutritional status and interferon response of close contacts in Delft, South Africa.

Study design and population: This is a community-based cross-sectional study. Eighty-six subjects between the ages of 18–65 years were included in the study of which 41 were household (HH) contacts and 45 non-household (NHH) contacts.

Methods: Each participant completed a structured questionnaire to obtain demographic information. Weight was measured to the nearest 0.1 kg and height to the nearest 1 mm. Three 1 ml blood samples were drawn for the QuantiFERON Gold In-Tube assay (QFT) and one 7 ml blood sample was drawn to determine ferritin status.

Results: Mean body mass index (BMI) of household contacts was 24.42 kg/m² (SD 4.629) and non-household contacts 25.53 kg/m² (SD 6.715). Of the household contacts 30 had a positive QFT response with a similar result of 32 in non-household contacts. There appears to be no significant relationship between BMI and QFT response of HH contacts ($P = 0.331$) or NHH contacts ($P = 0.069$). No significance was found between QFT and ferritin in both HH ($P = 0.565$) and NHH ($P = 0.073$) contacts.

Conclusion: Serum ferritin and BMI levels in HH and NHH tuberculosis contacts do not seem to influence QFT responses.

CLINICAL TB AND TREATMENT

PS-100920-13   Is a 4-month regimen adequate to treat non-cavitary tuberculosis after 2-month culture conversion?

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Background: The standard 6-month 4-drug regimen for treating drug-sensitive tuberculosis has cure rates of ≥95% in clinical trials, but the duration of the regimen is a major barrier to adherence, reducing efficacy and promoting the development of drug resistance. A recent trial evaluating a 4-month regimen of existing drugs in adults with non-cavitary TB and 2-month culture conversion was stopped early due to increased risk for relapse in the 4-month arm compared to the 6-month arm[1]. To contribute additional evidence, data from two published trials (Singapore, 1973 and East Africa, 1976) comparing 4 and 6 month regimens were analysed.

Methods: In both trials, all patients had isoniazid and rifampicin for 4 or 6 months with streptomycin and pyrazinamide in the first 2 months. Following the original trial reports, a per-protocol population was identified. Patients were separated into two subgroups: A) nil cavitation at randomisation and 2-month culture negativity and B) the remainder.

Results: In A, the relapse rate on the 4-month regimen was 5.8% with 0 on the 6-month regimen (risk difference 5.8%, 95%CI (1.3%, 10.4%)). In B, the relapse rate on the 4-month regimen was 14.1% compared to 1.6% on the 6-month regimen (risk difference 12.5%, 95%CI (7.9%, 17.1%).

Regimen	Duration	A. Nil cavitation and 2-month culture conversion		B. Cavitation or no negative culture at 2 months	
		n	Relapses	*n*	Relapses
2SHRZ/ 2HR(Z*)	4 months	102	6 (5.8%)	262	37 (14.1%)
2SHRZ /4HR(Z*)	6 months	63	0 (0.0%)	185	3 (1.6%)
Risk difference (95% confidence interval)		5.8% (1.3–10.4)		12.5% (7.9–17.1)	

* Some patients had supplementary pyrazinamide in the continuation phase.

Conclusions: Using no new drugs, the 4-month regimen was found to be inferior to the 6-month regimen, even in those with nil cavitation and 2-month culture negativity, supporting the results from the motivating trial. However, given that all patients relapsed with fully-sensitive strains it might be considered that the estimated 5.8% (albeit with a wide 95%CI (2.1%, 12.4%) is an acceptable relapse rate for a 4-month regimen meaning, based on these trial populations, that 27% of patients could be treated for only 4 months.

1 Johnson J, Hadad J, et al. Shortening treatment in adults with non-cavitary tuberculosis and 2-month culture conversion. Am J Respir Crit Care Med 2009; 18: 558–563.

PS-100452-13   Efficacy of populin use among TB patients with opisthorchosis for prevention of hepatotoxic side effects

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Background: Frequently the management of modern pharmacological anti-tuberculosis treatment is not feasible as a result of severe side effects. Most of anti-tuberculosis medications have serious hepatotoxic

impact. Our geographical region is endemic for opisthorchosis. Populin has anti-opisthorchosis, anti-inflammatory, choleretic, and hepatoprotective effects. Use of this medicine as a part of complex treatment for tuberculosis allows reducing frequency of hepatotoxic reactions. Clinical syndromes of infringements of functions of a liver include: a syndrome hepatomegaly, a painful syndrome; dyspeptic, cholestatic, citolytic. Preparation Populin' (firm 'Biolyt'of Tomsk) contains the concentrated water extract of a bark of an aspen and a dry concentrate of mineral water of lake Shira. The extract of a bark of an aspen contains phenolic glycozydes.

Methods: Under supervision there were 98 patients from 19 till 60 years, with diagnoses a tuberculosis of lungs and accompanying opisthorchosis. They have been divided into 2 groups. In the basic group of patients (56 persons) preparation Populin' was connected to traditional antitubercular therapy. In control group (42 persons) standard treatment was spent.

Results: It has been noticed, that at patients of the basic group hepatotoxic reactions were shown much less often. The Dyspeptic syndrome in the basic group was observed in 12.5% of cases, in control group at 42.8%. Hepatomegaly in the basic group it has been revealed at 5.3% of patients, and in group of the control at 21.4%. The Cytolytic syndrome is revealed in the first group at 12.5% of patients, in the second at 40.4%, a cholestatic syndrome at 9.5% and 19% accordingly.

Conclusions: Thus, inclusion of preparation Populin' in complex treatment of patients with a tuberculosis in a combination with opisthorchosis leads to reduction hepatotoxic side effects.

PS-100472-13 Effectiveness of alcohol interventions among TB patients in Tomsk Oblast, Russia

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Background: In spite of the high co-occurrence and excess mortality associated with alcohol use disorders (AUDs) among individuals with tuberculosis (TB), there are no studies evaluating effectiveness of integrating alcohol care into routine treatment for this disorder.

Methods: A randomized controlled trial began in July 2007 in Tomsk (Russia) to assess the effectiveness of Brief Counseling Interventions (BCI) and administration of Naltrexone, singly, or in combination, as components of tuberculosis (TB) care. The study popula-

tion includes adult patients with newly diagnosed TB and confirmed diagnosis of primary AUDs. All physicians in Tomsk TB service have been certified to deliver BCI. Naltrexone has been given under directly observed therapy (DOT) in combination with the Brief Behavioral Compliance Counseling.

Scope of the research: The study is successfully enrolling eligible subjects in the RCT to evaluate the relationship of integrating effective pharmacotherapy and brief behavioral intervention on TB and alcohol outcomes, as well as reduction in HIV risk behaviors. After two and a half years of the study, 164 patients have been enrolled out of 251 eligible (65%).

Conclusions: The proposed treatment strategy could be applied elsewhere in Russia and in other settings where TB control is jeopardized by AUDs. If demonstrated to be effective, this model of integrating alcohol interventions into routine TB care has the potential for expanded applicability to other chronic co-occurring infectious and other medical conditions seen in medical care settings.

PS-100936-13 Keeping clinical trials relevant in the face of changing guidelines: enrolling patients with HIV

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Background: A TB treatment trial is often designed more than 5 years before results become available. It is an ongoing challenge to ensure results remain relevant in the face of changing guidelines and practice. Recent WHO treatment guidelines for HIV recommend earlier ART initiation, including among all with active TB. Given HIV co-infection rates exceed 50% in high incidence areas, it is important to consider the potential impact of such changes on recruitment, outcomes and generalisabilty in TB clinical trials. Implications for TB study design in ongoing and future trials are presented.

Methods: Published and non-published data were reviewed to estimate incidence and mortality rates of patients with HIV-TB by CD4 count. Power calculations were made and options for optimising recruitment without undermining validity were generated and assessed in context of current and planned studies. National ART programme guidelines were reviewed and surveys sent to site staff to assess standard of care in trial clinics.

Results: In high incidence areas 75% of patients with HIV-TB may be excluded by a CD4 cut-off of 350 cells/μL compared to 50% by a 250 cells/μL limit. Mortality in patients with TB-HIV is significantly increased in those with very low CD4. Enroll-

ing such patients in trials can artificially inflate the number of treatment failures, reducing efficacy of experimental regimens. However, excluding patients with HIV reduces study result generalisability and affects recruitment. In addition, despite guidelines, ART programmes vary in thresholds for ART initiation.

Conclusions: Groups planning and conducting TB trials should pay attention to recruitment of HIV infected patients to ensure they are well represented in study populations, while remaining aware of the impact on outcomes and study power. For trials to be relevant and ethical it is important that study protocols are evaluated to ensure they fulfil aims in light of new research and changing guidelines.

PS-100031-13   Weight loss is an important risk factor for interruption of anti-tuberculosis drugs in liver toxicity

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Aim: Drug-induced hepatotoxicity (DIH) is an important complication of treatment of tuberculosis (TB); if severe, it may necessitate interruption of anti-TB medication. Because malnutrition might be a risk factor, we aimed to determine its contribution to interruption of anti-TB medication.

Methods: Retrospective observational study of 192 active TB patients consecutively admitted in a third-line Tuberculosis Center in the Netherlands, 2005–2008. The outcome measure for DIH was defined as necessitating interruption of TB drug treatment. Multivariate logistic regression analysis on interruption of anti-TB medication was performed, with age, gender, nutritional status, tuberculosis disease severity, drug resistance, co-morbidity including baseline liver functions, anti-TB medication regimen, co-medication and addictions as independent risk factors.

Characteristics of the study population	$n = 192$ (100%)
Age, mean ± SD	39.8 ± 16.6
Female	44 (22.9%)
Non-European origin	124 (64.6%)
Body mass index at start of anti-TB medication, mean ± SD	20.3 ± 3.9
Weight loss ≥2 kg after starting anti-TB medication	28 (14.6%)
Pulmonary TB	135 (70.3%)
Multidrug resistance	15 (7.8%)
HIV-positive	15 (7.8%)
Hepatitis B	3 (1.6%)
Hepatitis C	11 (5.7%)
Alcohol abuse	67 (34.9%)
Drug abuse	50 (26.2%)

Results: Anti-TB medication was interrupted in 31 patients (16.1%) of the population studied. The most important risk factor was weight loss of 2 kg or more within 4 weeks during TB treatment (OR = 211, CI = 36.0–1232). Other independent risk factors were infection with hepatitis C (OR = 19.6, CI = 2.4–164), age over 60 years (OR = 18.5, CI 2.3–151) and multi-drug resistant TB (OR = 8.2, CI 1.3–53.6).

Conclusions: Weight loss during TB treatment was the most important risk factor for DIH necessitating interruption of anti-TB medication. Prospective studies are needed to assess the cause-and-effect relationship between weight loss and an evolving DIH during TB treatment.

PS-100045-13   Outcome of hospitalized patients with tuberculous pleurisy: clinical impact of the disease extent

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Objectives: To analyze the clinical characteristics and in-hospital outcome of hospitalized patients for tuberculous pleurisy.

Methods: Patients who were hospitalized for pleural effusion (PE) of unconfirmed diagnosis and were finally diagnosed as tuberculous pleurisy were identified. We classified them according to the disease extent: isolated pleurisy (isolated pleurisy group) and pleurisy with pulmonary involvement (pleuro-pulmonary group).

Results: Of 205 had been hospitalized before the diagnosis was established, 51 (24.9%) belonged to the isolated pleurisy group. As compared with the pleuro-pulmonary group, the isolated pleurisy group was younger, had fewer underlying co-morbidities, and presented more frequently with fever and chest pain. Less patients in the isolated pleurisy group had hypoalbuminemia (<3.5 g/dL) and anemia. Regarding PE analysis, resistance pattern, and timing of anti-tuberculous treatment, the two groups were similar. After thoracentesis, patients who underwent pleura biopsy received anti-tuberculous treatment earlier than those who did not. The isolated pleurisy group had a lower in-hospital mortality and a shorter length of hospital stay.

Conclusion: In culture-confirmed tuberculous pleurisy, those with pulmonary involvement were associated with higher in-hospital mortality rate. Pleura biopsy was a rapid and sensitive examination which was associated with a better outcome.

PS-100067-13   Therapeutic drug monitoring in treatment of active tuberculosis

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Background: Therapeutic drug monitoring (TDM) is used to optimize dosing that maximizes therapeutic benefit while minimizing toxicity. In treatment of active TB, TDM is not routine yet low levels of anti-TB drugs are associated with worse treatment outcomes.
Methods: Data were collected by retrospective chart review of all active TB patients treated at the Montreal Chest Institute/Canada between 2004 and 2010. In a retrospective case control study, active TB patients in whom TDM was performed were considered cases, and compared to controls who did not have TDM, and were by year of diagnosis and results of direct smear microscopy. Medical records were reviewed to abstract demographic, clinical, radiographic, and microbiologic data including time until smear and culture conversion.
Results: In total, 20 patients were identified in whom TDM was performed, of whom 17 (87%) had at least one low drug concentrations. Overall 27 of 45 (60%) initial drug concentrations were low, and resulted in an increased drug dosage. Low levels were measured in these patients for 13 of 15 (87%) INH, 4 of 5 (80%) Rifabutine, and 8 of 12 (67%) rifampin, but only 2 of 13 (15%) PZA measurements. The 17 cases with low serum drug levels were more likely to have co-morbid illnesses, be smear positive, and have lower serum albumin compared to the 3 cases in whom all drug levels were within therapeutic ranges. Time to culture conversion was non-significantly longer.
Conclusions: Low drug levels were frequent in patients with active TB, particularly patients with HIV-infection or other co-morbidities. Therapeutic drug monitoring appears potentially useful in treatment of active TB, but is currently under-utilized.

PS-100112-13   Risk factors of drug-induced and virus-induced hepatitis during anti-tuberculosis treatment

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Context: Hepatitis during anti-tuberculous treatment (HATT) has been an obstacle in managing patients with tuberculosis (TB), especially in those with pre-existing liver disease.
Objective: We conducted this study to evaluate risk factors of HATT in patients with pulmonary TB, and clinical implications of serum viral loads in those with concomitant hepatitis B virus (HBV) or hepatitis C virus (HCV) infection.

Design, setting, and participants: We did a prospective observational study on patients with culture-confirmed pulmonary TB in a medical center. HATT was defined as an increase in serum aspartate transaminase (AST) or alanine transaminase (ALT) levels of >3 times the upper limit of normal (ULN) with symptoms, or an increase in serum AST or ALT levels of >5 times ULN without symptoms.
Main outcome measures: Incidence and risk factors for HATT.
Results: 360 TB patients (men: 232, 64.4%) were studied. The prevalence of concomitant HBV and HCV infection was 11.7% and 6.7%, respectively. HATT developed in 68 (18.9%) patients, with 59 (16.4%) being drug-induced, 5 (1.4%) HBV-induced, and 4 (1.1%) HCV-induced. Multivariate Cox proportional hazard regression analysis revealed that end-stage renal disease not under hemodialysis, N-acetyl-transferase (NAT2) slow acetylator, high initial HBV/HCV viral load, and women in those without HBV/HCV infection were significant predictors of drug-induced HATT, whereas end-stage renal disease not under hemodialysis and men in those with high initial HBV/HCV viral load were significantly associated virus-induced HATT.
Conclusions: Initial HBV/HCV viral load interacts with sex and, together with end-stage renal disease not under hemodialysis and NAT2 slow acetylator, were predictors of HATT. TB patients with these characteristics need close follow-up.
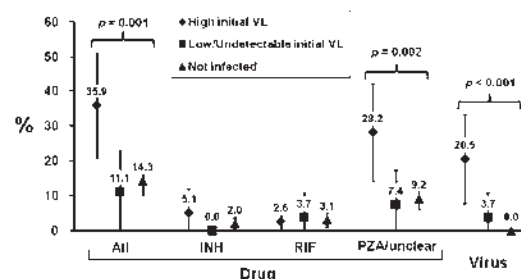
	All	INH	RIF	PZA/unclear	Virus
No. (%)	59 (16.4%)	8 (2.3%)	11 (3.1%)	40 (11.1)	9 (2.5%)
Onset (days): median [range]	34 [2 – 130]	21.5 [12 – 58]	31 [14 – 130]	35 [2 – 117]	31 [2 – 153]
Peak AST/ALT (ULN): median [range]	7.2 [3.6 – 47.3]	7.7 [5.8 – 28.7]	10.5 [3.7 – 13.0]	6.7 [3.6 – 47.3]	9.2 [3.7 – 25.5]

PS-100118-13   Plasma concentration of rifampicin, isoniazid and pyrazinamide in pulmonary tuberculosis and pleura

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Aim: To investigate plasma concentration of rifampicin, isoniazid, and pyrazinamide in pulmonary tuberculosis and pleural tuberculosis patients.

Methods: Determine plasma concentration of rifampicin, isoniazid, and pyrazinamide at 2 hours after administration in 168 tuberculosis patients by the HPLC method. Identify prevalence of low plasma concentrations of antituberculosis drugs

Results: There was a wide range of plasma concentration of rifampicin, isoniazid, and pyrazinamide of tuberculosis patients. The mean plasma concentration of rifampicin was 6.13 ± 4.66 μg/ml, of isoniazid was 2.99 ± 1.94 μg/ml, pyrazinamide was 38.98 ± 18.39 μg/ml. There was no significantly difference plasma concentration of rifampicin, isoniazid, and pyrazinamide in groups of pulmonary tuberculosis and pleural tuberculosis patients. Percentage of patients with plasma concentration below therapeutic concentration was 76.83% of rifampicin, 51.85% of isoniazid, 10.13% of pyrazinamide. There were 12.03% patients who had pyrazinamide concentration higher than therapeutic range.

Conclusions: There was a wide range of plasma concentration of rifampicin, isoniazid, and pyrazinamide of tuberculosis patients. Low plasma concentration of RMP and INH are common. It may be necessary to optimize drug dose by therapeutic drug monitoring, especially in patients with an inadequate clinical response to chemotherapy.

PS-100167-13   Drug-induced liver injury among tuberculosis patients in Mongolia

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Background: Elderly age, improper usage of alcohol and drugs, viral hepatitis infections are the most common affects of drug-induced liver injury (DILI). Three of the first-line anti-TB drugs, H, R and Z can cause DILI. Therefore DILI is happened during treatment in tuberculosis (TB) patients.

Objective: To assess the status of DILI among TB patients.

Method: A total of 250 smear positive TB patients with normal pretreatment liver function were monitored clinically as well as biochemically. We monitor liver function clinically and biochemically every month. Their data were collected on proforma and patients were treated with mixed dose combination of isoniazed, rifampicin, pyrazinamide and etambutol. Criteria of DILI are Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT) are >3 times upper limit of normal in the presence of symptoms.

Result: DILI was developed in 36 (14.4%) out of 250 TB patients. Average age of the DILI cases was 33.8 ± 13.26 (Cl 95% 17–83). Average starting period of the DILI was 19.95 ± 15.8 (2–57) after TB treatment. There were 19 (7.6%) cases which have hepatitis B carriers, 24 (9.6%) cases which have hep-

atitis C carriers. DILI developed 7 (36.8%) cases who were hepatitis B carriers, 4 (16.7%) cases who were hepatitis C carriers. A total of 32 (88.8%) cases had nausea, 30 (83.3%) cases had loss of appetite, 19 (52.7%) cases had vomiting and 17 (47.2%) cases had jaundice in DILI patients.

Conclusion:
1 Anti-tuberculosis DILI was developed in 14.4% of all TB cases.
2 DILI was found more often in hepatitis B carriers of TB patients ($P = 0.005$).
3 Most common symptoms among anti-tuberculosis DILI patients are nausea, loss of appetite, vomiting, and jaundice.

PS-100445-13   Functional polymorphism of cytokine genes during pulmonary tuberculosis

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Aim: Susceptibility to disease is determined by a combination of allelic variants of genes in the individual genotype forming unfavorable hereditary background, which is realized during the interaction with *Mycobacterium tuberculosis*. Here we studied the association between polymorphic variants of genes modulating the immune response and secretion of the corresponding protein products.

Methods: The study included 78 Caucasian individuals living in Tomsk, patients the Tomsk Regional Clinical Tuberculosis Hospital (46 men and 32 women, 19–35 years). The control group consisted of 82 healthy age- and sex-matched donors without history of pulmonary diseases. The results of genetic studies were analyzed by odds ratio (OR). Confidence intervals (95%) were calculated. The following conclusions were made: OR = 1, no relationship between factors; OR < 1, negative relationship between factors; and OR > 1, positive relationship between factors.

Results: Our results indicate that the course of infiltrative tuberculosis in residents of Tomsk and Tomsk region is accompanied by a decrease in the production of IL-2 by peripheral blood mononuclear cells. Secretion of IL-12 was shown to increase in these patients. The T (OR = 0.653) allele and homozygous TT (OR = 0.577) genotype of T-330G polymorphism in the IL2 gene and CC (OR = 0.5) genotype of A-1188C polymorphism in the IL12B gene are immunogenetic factors that have a protective activity against the susceptibility to pulmonary tuberculosis. The susceptibility to tuberculosis infection is associated with the G (OR = 1.532) allele and TG (OR = 1.792) and GG (OR = 1.306) genotypes of T-330G polymorphism in the IL2 gene and AC (OR = 1.65) genotype of the polymorphic region A-1188C in the IL12 gene.

Conclusion: Thus, the highest risk of infiltrative tuberculosis is associated with a combination of the GG

(OR = 1.306) genotype of T-330G polymorphism in the IL2 gene and AC (OR = 1.65) genotype of A-1188C polymorphism in the IL12 gene (GG/AC).

PS-100449-13 Factors associated with MDR-TB

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Background: In order to assess the leading factors associated with MDR-TB and, possibly, induced formation of resistant strains in patients with pulmonary TB, we have propose a null hypothesis that each of investigated social and clinical factors does not influence the development of MDR-TB.
Methods: We have tested the hypothesis using criterion χ^2 with Yates' correction. For those factors regarding which the null hypothesis has not proved to be true, Risk Ratio (RR) had been calculated for the purpose of describing a degree of risk of development MDR-TB at presence of those particular factors. The data from 118 patients were included in the analysis. Those patients had been placed on treatment in Tomsk TB hospital under the program DOTS-PLUS.
Results: Among the factors associated with MDR-TB, it is possible to allocate 2 main groups which demonstrate risks of social and clinical properties. In the first group one of the main factor is an existence of opiate dependency (RR = 6.11 (SD 4.08–8.12, $P <$ 0.0001), smoking (RR = 1.31 (SD 1.15–2.95, $P =$ 0.008), use of alcohol RR = 1.95 (SD 1.34–3.18, $P =$ 0.008), previous imprisonment (RR = 2.04 (SD 1.99–2.56, $P = $ 0.012), and presence of TB contact (RR = 2.10 (SD 0.13–4.07, $P <$ 0.0001). The group of clinical risk factors include some health history data, such as presence of certain concomitant conditions (type 2 diabetes mellitus RR = 3.12 (SD 1.14–5.09, $P = $ 0.044), a virus hepatitis B, C, or B+C with a liver cirrhosis RR = 8.57 (SD 1.64–44.86, $P =$ 0.018), mental disorders secondary to alcohol dependence RR = 2.38 (SD 0.97–5.83, $P = $ 0.002), and expressiveness of TB inflammation detected by X-ray (more than two segments $\chi^2 = 6.40$, $P = 0.040$; lung tissue destruction $\chi^2 = 50.03$, $P < 0.0001$), and intensive bacterial shedding, confirmed by culture $\chi^2 = 19.75$, $P < 0.0001$).

PS-100450-13 Vitamin A and zinc supplementation and treatment outcomes in pulmonary TB: a controlled trial

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Aim: To assess the efficacy of vitamin A and zinc supplementation on sputum smear and culture conversion and time to culture detection (TTD) among new cases with pulmonary TB.
Setting: Delft, South Africa.
Methods: Subjects were randomized to receive a single dose of 200 000 IU of retinyl palmitate or matching placebo within 24 hours after the start of standard TB therapy. They also received 15 mg zinc or placebo daily for 8 weeks. One early morning sputum specimen was collected from each participant every week for auramine stain and cultured on liquid media (BACTEC MGIT 960). Other data include performance status, chest X-rays, nutritional and biochemical parameters. Statistical analyses were carried out using SAS 9.2 and Stata 9.0.
Results: Seventy seven patients were randomized to the intervention and control groups, respectively. Twenty were HIV-positive (13%) and 12 patients had an unknown HIV status (8%). The date of culture or smear conversion was taken as the date of the first negative culture or smear if there were no subsequent positive cultures or smears. Kaplan Meier analysis demonstrated no differences in the time to smear or culture conversion between the treatment groups during the 8 week period ($P = 0.15$; $P = 0.38$; log rank test). Log-logistic regression analysis found no significant group interaction effect over the 8 week period in terms of TTD ($P = 0.32$). For both groups, baseline TTD was a significant contributor to TTD at week 8 ($P < 0.0001$). After 2 months there was a significant reduction in the total number of patients with lung cavities (< 5cm) in both groups (OR = 0.56, 95%CI 0.32–0.55). Weight gain was similar in the 2 treatment groups (2.3 ± 3.5 kg vs. 2.2 ± 2.4 kg; $P = 0.68$).
Conclusion: Supplementation with vitamin A and zinc did not affect treatment outcomes of patients with pulmonary TB after 2 months.

PS-100662-13   Characterization of Mce4A protein of *Mycobacterium tuberculosis* role in invasion and survival

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Background: The mce4 operon is one of the four homologues of mammalian cell entry (mce) operons of *Mycobacterium tuberculosis* The mce4A (Rv3499c) gene within this operon is homologous to mce1A (Rv0169), that has a role in host cell invasion by *M. tuberculosis.*
Design: We have cloned and expressed mce4A along with mce1A genes in E. coli. Moreover we have also purified Mce4A as well as Mce1A proteins.
Results: By transmission electron microscopy we have demonstrated that recombinant Mce4A protein facilitates the invasion of non-pathogenic strain of E. coli into non-phagocytic HeLa cells. We observe that mce4A gene has a role comparable to mce1A in the survival of recombinant E. coli in human macrophages. During our study we have found that Mce4A protein when overexpressed in E.coli form inclusion bodies, Mce4A protein was solubilised, purified and refolded from the inclusion bodies. The refolded Mce4A was biologically active as demonstrated by transmission electron microscopy. The recombinant protein retained cell entry function as the latex beads coated with Mce4A protein were able to enter the non-phagocytic HeLa cells. Using antibodies raised against Mce4A protein, we show that the protein is localized in the cell wall fraction of *M. tuberculosis* H37Rv stationary phase culture only.
Conclusion: Mce4A protein is expressed during the stationary phase of broth culture and localizes in the cell wall fraction of *M. tuberculosis.* Mce4A protein expressed in non-pathogenic E.coli enables it to enter and survive within HeLa cells and the macrophages. As Mce4A protein is expressed during later phase of mycobacterial growth, our results raise the possibility of it playing a role in maintenance of persistent tubercular infection.

PS-100674-13   Disease characteristics of TB patients: a retrospective cohort study of smokers versus non-smokers

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Background: The association between smoking and tuberculosis (TB) is increasingly coming to light. The present study was to compare disease characteristics of smoking versus non-smoking TB patients in Penang, Malaysia.

Methods: A retrospective cohort study comparing the clinical characteristics of TB patients who were smokers versus non-smokers was conducted. The data were extracted from medical records of newly diagnosed TB patients who registered at a chest clinic of Penang General Hospital between 1 January 2006 and 30 June 2008.
Results: There were 1017 TB patients whose smoking status was known. Of these, 493 were excluded from the analysis, as they did not satisfy the eligibility criteria of the study. As a result, 524 TB patients were included in the analysis (274 ever smokers versus 250 never smokers). Ever smokers were significantly more likely to present with weight loss (OR 2.37, CI = 1.64–3.43), productive cough (OR 3.70, CI = 2.44–5.61), dyspnea (OR 3.74, CI = 2.04–6.83) and loss of appetite (OR 2.67, CI = 1.87–3.81), but were less likely to have other extrathoracic symptoms on presentation (OR 0.54, CI = 0.35–0.84). In addition, ever smokers had increased likelihood of lung opacity on CXR (OR 6.74, CI = 3.33–13.60) and were about 2 folds more likely to have initial positive sputum smear (OR 2.41, CI = 1.67–3.47). Presence of initial positive sputum culture and effusion on CXR did not differ between smoking and non-smoking TB patients.
Conclusion and recommendations: Smoking showed a considerable association with lung involvement. This association also had significant effect on the severity of clinical picture, radiological and microbiological findings resulting in more aggressive TB. Smoking was associated with worsening of TB patients' prognosis resulting in more severe symptoms. Therefore, tobacco cessation interventions should be delivered to all TB patients who are smokers when they are receiving TB treatment.

PS-100682-13   Les pneumopathies communautaires en hospitalisation en milieu pauvre : quels facteurs de gravité ?

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Introduction : Les infections respiratoires sont la deuxième cause de morbidité et de mortalité au Burkina Faso. Le service de Pneumologie du CHU Sourô Sanou est le service de référence de ces pathologies de la moitié sud du pays. En vue de contribuer à une meilleure prise en charge des cas, nous avons mené cette étude.
Patients et méthodes : Nous avons étudié de façon prospective, les dossiers de 90 patients hospitalisés pour pneumopathie communautaire dans le service de Pneumologie entre le 1er janvier et le 31 décembre 2009. Ont été recherchés les facteurs de gravité des pneumopathies communautaires, l'évolution clinique, le mode de sortie.

Résultats : La durée moyenne d'hospitalisation a été de 15 jours. Les facteurs de gravité souvent associés retrouvés étaient infection à VIH (12 fois), âge supérieur à 65 ans (24 fois), bas niveau socio économique (70 fois), long itinéraire thérapeutique (22 fois), retard diagnostique (15 fois), troubles de la conscience (05 fois), lésions étendues (52 fois), pleurésie para pneumonique (17 fois). Les patients sont sortis du service selon les modes suivants guérison (67 cas), décès (19 cas), sans avis médical (4 cas).

Discussion : L'infection à VIH et le bas niveau socio économique (avec ses corollaires) ont été les principaux facteurs de gravité. Dans notre contexte d'exercice ces deux facteurs sont en synergie négative, expliquant la forte létalité. La prise en charge tardive et inadéquate a aggravé le pronostic.

Conclusion : Les pneumopathies communautaires constituent une menace sanitaire. La formation des praticiens du niveau sanitaire de base évitera la forte létalité et les complications.

PS-100687-13   La tuberculose en hospitalisation dans un service de référence au Burkina Faso

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Introduction : La tuberculose est un problème de santé publique au Burkina Faso. Le service de Pneumologie du CHU Sourô Sanou est un service de référence pour la prise en charge des cas graves de tuberculose. En vue de contribuer à une meilleure prise en charge des cas, nous avons mené cette étude.

Patients et méthodes : Nous avons étudié de façon prospective, les dossiers des patients hospitalisés pour tuberculose dans le service de Pneumologie entre le 1er janvier et le 31 décembre 2009. Le diagnostic de tuberculose a été fait sur la combinaison de façon variable de l'histoire clinique, la radiographie thoracique, la bacilloscopie, la biopsie pleurale, la culture mycobactérienne et l'évolution clinique favorable sous anti tuberculeux.

Résultats : Au cours de la période, 166 cas de tuberculose ont été hospitalisés parmi lesquels on comptait 48 miliaires tuberculeuses, 40 pleurésies, 41 TPM+ (dont 6 cas de tuberculose multi résistante), 23 TPM− et 14 cas multi viscérales. La prévalence VIH chez ces patients était de 28.3 %. La létalité tuberculeuse était de 9.7%.

Discussion : La tuberculose est la deuxième cause d'hospitalisation dans le service. Elle continue d'être la principale infection opportuniste au cours de l'infection à VIH. La survenue de cas à bacilles multi résistants est une menace et traduit des faiblesses dans la prise en charge des cas ordinaires.

Conclusion : Le diagnostic et la prise en charge des cas graves de tuberculose nécessitent un équipement performant dont ne dispose pas régulièrement le service de Pneumologie du CHU Sourô Sanou.

PS-100928-13   Tuberculosis en el área de influencia de un hospital general. Evolución en 5 años

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Objetivos: Estudiar las tuberculosis (TB) diagnosticadas en un hospital de referencia de 197.272 habitantes (35.927 inmigrantes).

Método: Revisión de 115 TB diagnosticadas de 01/2005 a 10/2009. Características, tratamiento y cumplimiento.

Resultados: El 63.5% eran varones. Edad media 42.9 (3 meses 93 años). 44 inmigrantes (38.26%). (Europa del Este 9.6%, América Latina 8.7%, Marruecos 14.8%, resto África 2.6%, Asia 1.7%, Europa Occidental 0.9%). Casos pediátricos 9 (3 autóctonos, 6 hijos de inmigrantes). Encontramos un aumento progresivo del número de inmigrantes por año (ver tabla). Se diagnosticaron 66 TB Pulmonar (57.39%), 14 Pleural (12.17%), 8 Linfática Torácica (6.9%), 3 Miliar (2.6%), 1 Pleuropulmonar (0.87%) y 23 Otras (20%). Esta distribución no ha variado de forma significativa en los 5 años. Fueron hospitalizados 64 (55.65%). La utilización de 3 drogas/6 meses (3D/6M) ha disminuido del 60% (2005) al 14.28% (2009).

Resistencias: 6.9%: 1 Isoniazida (H), 1 Rifampicina (R), 1 Pirazinamida (Z), 3 multirresistentes (MDR-TB) y 2 de extrema resistencia (XDR-TB). Las XDR-TB eran de Europa del Este. De las MDR-TB, 2 autóctonas y 1 procedente de África. Las resistencias a H y R eran autóctonas y la de Z de América Latina. Se modificó el tratamiento en 3 casos por toxicidad hepática y 2 por alergia a H. Se curaron 92 pacientes (80%), 2 murieron por TB; 6 por otras causas, 12 se perdieron (10.43%) y 3 se trasladaron a su lugar de origen.

	2005	2006	2007	2008	2009
Casos TB	35	14	28	31	7
Autóctonos	21	11	20	16	3
Inmigrantes	14	3	8	15	4
	(40%)	(21%)	(28,57%)	(48,38%)	(57,15%)

Conclusiones: Nuestra incidencia de TB se ha mantenido estable, con aumento progresivo de inmigrantes. No observamos incremento en niños, aunque predominan los hijos de inmigrantes. En las resistencias únicamente encontramos diferencias entre autóctonos e inmigrantes en las XDR-TB, procedentes de

Europa del Este. El abandono progresivo de la pauta 3D/6M concuerda con las directrices actuales y el aumento de resistencias. Es necesario aumentar el control de los pacientes para disminuir la proporción de perdidos.

PS-100998-13   How long does it take for TB treatment to be started in infectious TB patients in Bulawayo, Zimbabwe?

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Background: Tuberculosis (TB) case finding and holding are decentralised to 18 municipal clinics in Bulawayo. The objective of the study was to measure the number of days required for a person presenting with symptoms suggestive of TB and who is found to have sputum smear-positive TB to be commenced on TB treatment.
Method: All TB suspects recorded in the registers with positive diagnostic smear result (s) from 1 January to 31 December 2009 at four clinics were line listed. The dates of presentation, sputum collection, receipt of results and starting of treatment were recorded and intervals analysed.
Results: A total of 121 TB suspects (55% female) were recorded during the study period. Dates were incomplete for two patients. The interval between attendance and start of treatment ranged from 1 to 64 days. Forty four (38%) and 28 (24%) patients were started on treatment 6–10 and 1–5 days after initial consultation, respectively. Twenty two (18%) patients were started on treatment between 11 and 25 days. Twenty one patients were not started on TB treatment at all: four (3%) were found to have died and 17 (14%) had either left the city or could not be found at given address. The longest interval contributing to delayed start was the period between specimen collection and receipt of the results: 60 (50%) patients waited for more than 5 days.
Conclusion and recommendations: Slow sputum microscopy turn-around was found to contribute to health service related delay in this study. Many suspects were confirmed to have TB and commenced on treatment within acceptable period though some could not be found at given addresses. It is essential that the department ensures sufficient supply of sputum containers, reliable transport between clinics and microscopy laboratory and strengthens communication between health providers and TB suspects so that they appreciate time required for investigations and provide accurate addresses.

PS-101006-13   The probability of detecting urogenital TB in persons with signs of post-pulmonary TB

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Goal: To estimate the probability of detecting urogenital TB in persons who have post pulmonary TB signs on the background of any chronic non-specific urological disease.
Material and methods: There were 114 cases enrolled in the study. Persons who treated in the URIPP in purpose of differential diagnostics of urogenital TB. All of them were under dispensary control for the long time (over 5 years). In them: males 49.1%, females 50.1%. Most of them (57.9%) were elder than 50. Abovementioned is equal to structure of patients with urogenital TB in Urals. Patients, anamnesis, results of current and previous examinations and other medical records were investigated.
Results: Over 25% of them had significant contact with smear positive TB case, 16.3% had post-pulmonary TB signs and 25.4% had had an active pulmonary TB on the moment of the study. In 46.3% of patients were under long-lasting dispensary control because of non-specific chronic urological disease, such as pielonephritis, cystitis and etc. But there was not specific examination for TB performed before they had come to the URIPP. That's why in 31% of cases disease were detected in a tardy stages. Urogenital TB was developed in them meanly in 10.5 (CI 5.5; 16.0) years after pulmonary TB. Isolated renal TB was detected in 34.2% and in 65.8% there was combination of processes; 25.4% with collaboral ureter TB, 20% with TB of the bladder and in 19.7% genital TB.
Summary: The probability of detecting urogenital TB in patients who have post pulmonary TB signs on the background of any chronic non-specific urological disease is 3.92 higher (OR, $P < 0.05$) than in other groups of patients. During dispensary control in general health facility for chronic non-specific urological disease most of patients had had signs of pulmonary TB but nobody paid attention on that, that's why over 65% in them had large and tardy detected urogenital TB.

PS-101046-13 Clinical, microbiological and micronutrient profile of paediatric intrathoracic TB patients in Delhi

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Aim: To assess the clinical, microbiological and micronutrient profiles of children with intrathoracic tuberculosis (TB).

Setting: Tertiary care hospital New Delhi, India.

Methods: Children (6 months–14 years) with intrathoracic TB were enrolled and their baseline clinical, microbiological and micronutrient (zinc and copper) profile assessed.

Result: A total of 195 children were studied; median age 103 (IQR 62–144) months, male 43%, BCG vaccinated 68%, TB contact history in 36%. Presenting symptoms were cough (60%), fever (72%), weight loss (61%) and lymph node swelling (15%). Weight for age z-scores were <-3 in 80 (41%) children. Disease classification on chest radiograph included primary complex (PC, 29%), progressive disease (PD, 54%) and pleural effusion (PE, 17%). No association was seen between malnutrition, BCG status and intrathoracic disease classification (PC/PD/PE). Acid fast bacilli (AFB) were identified by microscopy in 19 and 15 patients in gastric aspirate (GA) and induced sputum (IS), respectively. *M. tuberculosis* was identified on culture in 51 and 20 patients in GA and IS respectively [kappa 0.2 (95%CI 0.07–0.340]. Of 133 children tested, serum zinc was low (<60 μg/dL) in 47 (35.4%) and copper levels elevated (>150 μg/dL) in 75 (57%). AFB positivity was associated with low serum zinc levels (OR 2.77, 95%CI 1.27–6.06) and elevated serum copper levels (OR 2.87, 95%CI 1.27–6.49).

Conclusion: Clinical symptoms of TB in children are non-specific. Mycobacterial yield from ambulatory gastric aspiration is superior to induced sputum. AFB positivity was associated with low serum zinc and elevated serum copper levels.

PS-101215-13 Cholesterol uptake in *M. tuberculosis*: the role of Mce4A (Rv3499c) protein

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Background: It is generally accepted that *M. tuberculosis* primarily invades and replicates within alveolar macrophages during the course of infection and progression of tuberculosis. The sequencing of the complete genome of *M. tuberculosis* has revealed the presence of four different mce operons sharing significant homology. Recently, we have demonstrated that mce4A (Rv3499c) gene of mce4 operon has a role in invasion and survival of the pathogen (Saini et al., 2008). It is also reported that the strains lacking Mce4 proteins have drastically reduced ability to acquire and metabolize cholesterol in vitro which helps in its growth (Pandey et al., 2008). Bioinformatically Mce4A protein can act as a substrate binding protein during import of substrate.

Design: In this report we have concentrated on the investigation of the role of Mce4A protein as a substrate binding protein.

Results: Spectral analysis of cholesterol binding and analysis of growth of mycobacteria in presence of cholesterol revealed that Mce4A protein efficiently binds to cholesterol and enhances its in vitro growth. Using radiolabeled cholesterol we further confirmed the role of Mce4A protein in cholesterol uptake.

Conclusion: These studies reveal that Mce4A gene plays a pivotal role in cholesterol uptake in *M. tuberculosis*.

PS-101516-13 Does *M. tuberculosis* lineage influence pulmonary impairment?

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Background: Over the past decade there have been many advances in the molecular characterization of the genomes within the *M. tuberculosis* complex. Based on phylogenetic markers, strains can be segregated by ethnic populations and geography. We hypothesized that persons infected with sympatric strains would have less pulmonary impairment after tuberculosis (PIAT) than those infected with allopatric strains.

Methods: We performed a prospective study to determine if *M. tuberculosis* lineage influenced post tuberculosis impairment in treated patients. Pulmonary

function tests (PFT) were performed on all culture-confirmed pulmonary tuberculosis patients who had completed >20 weeks of DOT in Tarrant County, Texas between 7/2005 and 12/2009. PIAT was graded in accordance with established American Medical Association guidelines. *M. tuberculosis* lineages and families were based on spoligotype information from the U.S. National TB Genotyping Service. Stepwise logistic regression methods that included lineages were used to determine significant independent predictors for pulmonary impairment.

Results: Overall, half of patients had pulmonary impairment, with varying levels of severity across lineages and in racial/ethnic populations. *Euro-American* was the frequent lineage, 168/281 (59.8%) equally encountered by foreign-born and U.S.-born persons. *East-Asian (Beijing)* was found in 57 out of 281 persons (20%) but contributed 71% of PIAT among U.S.-born patients. In multivariate logistic models that controlled for lineages, the odds for PIAT were 6 times higher for Blacks and 250 times higher for Caucasians than Asian persons.

Conclusions: These data suggest that PIAT frequency and severity varies with lineage among distinct ethnic populations. These findings have important clinical, therapeutic and policy implications for tuberculosis control.

DIAGNOSIS OF LATENT TB INFECTION AND IMMUNOPATHOGENESIS OF TB

PS-100125-13   Serum concentrations of cytokines and chemokines in lung tuberculosis patients

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Introduction: Resistance or susceptibility to mycobacterial infection is mediated by macrophages, T cells and their interactions. These cells are dependent on the interplay of cytokines and chemokines produced by each cell. CD4+ T cells are considered to consist in two subsets: Th1 cell, considered important in macrophage function by induction with IL12, and Th2 cell which is able to produce IL4, IL9 and is induced by CCL18.

Patients and methods: Serum was obtained from 24 patients with pulmonary active tuberculosis before treatment. Mean age was 32 years and 70% were male. The patients were attended at the Universidad Veracruzana Health Center in Coyopolan. There was no difference in ethnic origin.

Assays: Detection of IL4, IL12, IL9, CCL2, and CC18 was measured in serum by ELISA using recombinant antibodies MOAD, according to the manufacturer's

(R&D Systems) instructions. The mean concentration IL4 was 95 pg/ml IL9 238 pg/ml IL12 was 24 pg/ml, CCL2 84 pg/ml and CCL18 1176 pg/ml.

Discussion: We found significantly raised levels of CCL18, IL4 and IL9 accompanied by weight loss, fever and malaise. These mediators have a role in the Th2 response and progression of the disease. The decreased IL12 and CCL2 that are associated with susceptibility.

PS-100329-13   Some characteristics of immune response in primary pulmonary tuberculosis patients with diabetes

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Design: A cross-prospective study on some characteristics of immune response in primary pulmonary tuberculosis patients combined with diabetes mellitus.

Objectives: 130 AFB (+) primary pulmonary TB patients with diabetes (TBDM) and 130 AFB (+) primary pulmonary TB patients without diabetes (TB) treated at National Hospital of Tuberculosis and Lung Disease; 30 healthy people to compare some immunological indicators.

Results: The rate of negative mantoux test in TBDM patients is higher than in TB patients (23.8% vs. 13.1%, $P < 0.01$). On the other hand, the rate of positive IgG response to tubercle sonicated antigen in the TBDM group is lower than in the TB group (60.0% vs. 83.3%, $P < 0.05$). IgA response to the sonicated antigen is not different significantly (66.7% vs. 56.7%, $P > 0.05$). Capacity of IL-2 and TNF-α production of the peripheral blood cells decreased in TBDM patients compared to TB patients ($P < 0.05$). This capacity in those two groups of patients were lower than healthy persons ($P < 0.05$), the corresponding concentration of IL-2 and TNF-α in three groups was: 45.17 ± 22.08 pg/ml; 56.65 ± 30.33 pg/ml; $67.74 \pm 2, 69$ pg/ml and 414.72 ± 306.37 pg/ml; 545.9 ± 260.82 pg/ml; 648.4 ± 30.51 pg/ml, respectively.

Conclusion: The immune response in TBDM patients is weaker than TB patients.

PS-100390-13   Endogenously activated Th1/Th2 cytokines differentiate recent and past tuberculosis infection

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Aim: Tuberculin Skin Test positivity (TST+) rate in the Pakistani population with wide BCG coverage is between 40–50% and up to 80% in recently exposed

household contacts. The diagnostic value of TST is therefore questionable in both patients and exposed contacts. Endogenously activated immune cells are present in the peripheral blood compartment of TB patients. Similar cellular activation may also be occurring in recently infected household contacts. However, cytokine signatures may be different in different groups and may distinguish active disease, recent and past infection.

Methods: Whole blood was cultured for 2 days and spontaneous secretion of Th1/Th2 cytokines were assessed in supernatants of TB patients (N = 54; pulmonary = 26; extrapulmonary = 28), recently exposed household contacts (HC = 27) and TST+ non exposed endemic controls (EC+ N = 18) using Multiplex Cytometric Bead Array (CBA). Mann-Whitney U tests were applied to evaluate differences in different groups.

groups	N	BD supIL2	BD sup IL4	BDsup IL6	BD sup IL10	BD supTNFa	BD sup IFNg
HC	27	-	-	++	++	(+)	++
PTB	26	++++	++	++	++++	+++	++++
ETB	28	+++++	++++	-	+++	-	++

p>0.05= (-); <0.05=+; 0.001++; <0.0001=+++; <0.00001++++; <0.00001=0+++++

Figure   Intensity of signal compared to EC TST+. HC = recently infected household contacts; PTB = pulmonary tuberculosis; ETB = extra pulmonary tuberculosis.

Results: Compared to EC+, TNFα (P = 0.006), IL10 (P = 0.000001), IFN-γ (P = 0.0002), IL2 (P < 0.000001) and IL4 (P = 0.00002) were significantly raised in patients with active tuberculosis; TNFα (P = 0.01), IL10 (P = 0.0002) and IFN-γ (P = 0.0001) in the absence of IL2 and IL4 was associated with recent infection.

Conclusion: Such cytokine signatures may be very useful in differentiating recent and remote infection in a BCG vaccinated population.

PS-100697-13   Simple improvement of cell culture conditions significantly augments IP-10 and INF-γ responsiveness

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Objective: To identify simple methods for improving performance of cell mediated immune response (CMI) assays.

Materials and methods: Whole blood was incubated 18 h with TB10.4 peptide antigens or PHA mitogen at 37°C or 39°C in the presence of IL-10 blocking mAbs (aIL-10) and IL-7. All modifications were tested alone and combined. IP-10 levels were measured using an in-house ELISA and IFN-γ using the QuantiFERON ELISA.

Results: 23 TB10.4 responders and 11 non-responders were identified based on IP-10 levels under normal incubation conditions. In responders, incubation at 39°C increased the TB10.4 induced IP-10 levels (4153 vs. 5632 pg/ml, P = 0.03), but not IFN-γ levels (54 vs. 55 pg/ml, P = 0.68). PHA responses were increased at 39°C for both IP-10 (8066 vs. 11030 pg/ml, P = 0.04) and IFN-γ (235 vs. 300 pg/ml, P = 0.04). Adding IL-7, especially with aIL10, increased the levels of both TB10.4 and PHA induced IP-10 and IFN-γ (P < 0.01 for all). The effect of adding IL-7 and aIL-10 on TB10.4 response was stronger when incubating at 39°C for both IP-10 (5432 vs. 12449 pg/ml, P < 0.01) and IFN-γ (102 vs. 112 pg/ml, P = 0.04) suggesting synergistic effects. Non-responders did not respond to TB10.4 under any incubation conditions.

Conclusions: Incubation at 39°C increases the induction of IP-10 and IFN-γ after antigen and mitogen stimulation, especially with IL-7 and aIL-10. Simple modifications improve CMI assay performance and may improve sensitivity in diagnostic tests for *M. tuberculosis* infection.

For the conference, we will also present the effects of the modifications applied to the Quantiferon test in a cohort of 10 TB patients.

PS-100950-13   The significance of the antigen-specific IFN-γ release assay in vitro for differential diagnosis

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Setting: The significance of the antigen-specific interferon-gamma (IFN-γ) release assay in vitro for differential diagnosis between nontuberculosis inflammatory lung diseases and tuberculosis (TB) patients.

Background: The significance of IFN-γ release assay in countries with high tuberculosis prevalence is still unclear. In some cases of TB diagnosis there are difficulties of differentiation with nontuberculosis inflammatory lung diseases.

Objectives and methods: Using enzyme-linked immunoassay developed by us and aimed for measuring IFN-γ cell response to *M. tuberculosis* antigens (tuberculin PPD and specific antigen ESAT-6) in whole blood samples after 24 hour incubation, we have studied 2 groups of patients: 60 TB patients aged 19–66 yrs. and 44 patients with nontuberculosis inflammatory lung diseases aged 17–76 yrs.

Results: In patients with nontuberculosis inflammatory lung diseases and TB patients IFN-γ levels in

whole blood 95%CIs for response to PPD were 113.7–282.7 pg/ml versus 236.9–367.4 pg/ml ($P < 0.0005$ Mann-Whitney U-test); while the respective 95%CIs for ESAT-6 were 35.9–154.4 pg/ml versus 59.3–126.3 pg/ml ($P = 0.013$ Mann-Whitney U-test). When using 70 pg/ml as a cut-off point, with nonTB inflammatory lung diseases 79.5% patients had no IFN-γ response to ESAT-6 and 47.7% patients had no IFN-γ response to PPD as compared with 66.7% and 20% TB patients who had no response to ESAT-6 and PPD consequently. The diagnostic accuracy of this test is 66.4%. In case of IFN-γ release lower than 70 pg/ml odds ratio for nonTB inflammatory lung diseases is 3.7. The positive predictive value is 63.6% (95%CI 48.4–77.2) and the negative predictive value is 67.6% (95%CI 60.4–73.9%, $P < 0.001$).

Conclusion: The significance of the antigen-specific IFN-γ release assay in differential diagnosis between TB and nonTB inflammatory lung diseases is not so high as we need in the clinical practice. Probably it is due to high level of the latent tuberculosis.

PS-101438-13   An in vitro assay of anti-mycobacterial immunity predicts nutritional risk factors for tuberculosis

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Background: A blood test to predict TB susceptibility would facilitate the targeting of appropriate interventions to those at greatest risk.

Methods: We optimised a whole-blood assay of human anti-mycobacterial immunity. Luminescent mycobacteria were added to 839 whole-blood samples from healthy volunteers at risk of TB in Peru. The samples were incubated for 96 hours at 37°C and a portable luminometer was used to measure whether the participants' blood killed or supported mycobacterial growth. The results were analysed for nutritional associations.

Results: Median body weight was 60 kg, 505 (60%) were female and the median age was 28 years. Indicators of poor nutrition were strongly associated with increased growth of mycobacteria in whole blood. Thus blood from malnourished individuals had impaired immune restriction of mycobacterial growth. Specifically, in linear regression analysis, the standardised beta-coefficient for body mass index was -0.17 ($P < 0.001$). There were similar associations with both body fat (-0.15, $P < 0.001$) and body protein stores (-0.17, $P < 0.001$), see Figure. These associations were maintained after adjusting for age, sex and previous TB diagnosis ($P < 0.001$ for all associations). There was a strong positive association between body density (but not body weight) and the growth of mycobacteria in whole blood, implying increased susceptibility to TB, in both adjusted and unadjusted analysis.
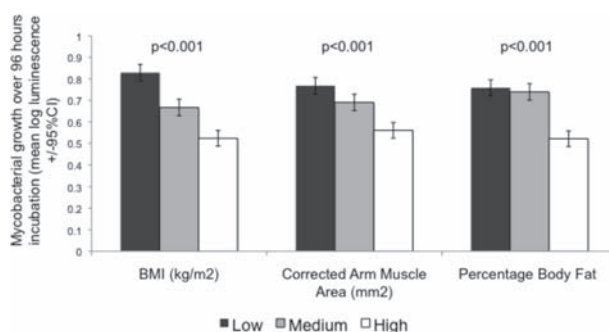
Figure   Mycobacterial growth in whole blood: the effect of nutrition.

Conclusions: Poor nutrition has one of the largest evidence bases as a risk factor for TB. We found that a simple in vitro assay of whole blood restriction of mycobacterial growth demonstrated this association between poor nutrition and TB susceptibility and provided evidence for mediation by both protein and calorie nutrition. This provides insights into nutritional determinants of TB susceptibility and indicates that this assay may help to identify individuals most at risk of TB and enable evaluation of interventions aiming to reduce TB susceptibility.

PS-100087-13   Evaluation of the QuantiFERON TB Test (QFT-TB) in detection of children infected with *Mycobacterium tuberculosis*

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Introduction: Recently a new diagnostic test (Quantiferon-TB Gold) which measures the production of interferon gamma in whole blood has been introduced. The aim of this study is to compare the performance of the IFN-gamma assay with Tuberculin skin test for the identification of latent TB infection in childhood in the Pediatric Pulmonary Ward of Masih Daneshvari Hospital.

Material and methods: The present cross-sectional study was conducted on 100 children, aged 2 months 15 years during 2007–2008. Children were divided into three groups of Case, Contact and Control. Whole blood was collected for measuring Interferon-gamma using Quantiferon-TB Gold kit In this procedure, *Mycobacterium tuberculosis* specific antigens (ESAT-6 and CFP-10) were used.

Result: Smear of the gastric washing (3×) was pre-

pared in all groups; 30% of the Cases were AFB positive, while all of the Contact groups had negative smears. Positive PPD test was observed in 90% of the Cases and 24% of the Contacts. Out of 50 contact cases 18 (36%) showed positive QFT test, and in 20 TB patients 18 (90%) had positive test.

Conclusion: To our knowledge, this is the first study to investigate the performance of the whole blood IFN-gamma assay in diagnosing latent TB infection in children in Iran. Our study has high lighted fair and moderate agreement in contact and TB group respectively between the TST and QFT-TB test in children More studies are required to clarify this relationship.

PS-100362-13 Antibodies against immunodominant antigens of *Mycobacterium tuberculosis* in US tuberculosis suspects

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Background: The immunodominance of *Mycobacterium tuberculosis* proteins Malate Synthase (MS) and MPT51 has been demonstrated in case-control studies with patients from tuberculosis (TB)-endemic countries. The value of these antigens for serodiagnosis of active TB is now evaluated in a cross-sectional study of pulmonary TB suspects in the US diagnosed to have early stages of TB, HIV associated TB, or other respiratory diseases (ORD).

Methods: Consecutive subjects with a high clinical suspicion for TB were enrolled in a cross-sectional study from September 2006 to October 2008 from 4 public hospitals in New York City, New York. Serum antibody reactivity to recombinant purified MS and MPT51 was determined by ELISA in TB suspects and well-characterized control groups. The gold standard for TB diagnosis was a respiratory specimen culture positive for *M. tuberculosis*, or if culture-negative, clinical and radiologic response to antituberculous therapy. Subjects were categorized as ORD if they had a respiratory culture negative for *M. tuberculosis*, and an ORD diagnosis as per physician's discharge note.

Results: TB suspects were diagnosed with TB ($n = 87$, 49% sputum microscopy negative, 90% culture confirmed, 20% HIV+) or ORD ($n = 63$, 58% HIV+). Antibody reactivity to MS and MPT51 was significantly higher in US HIV+/TB compared to HIV-TB ($P < 0.001$), and significantly higher in both TB groups compared to latent TB infection ($P < 0.01$). Antibody reactivity to both antigens was higher in US HIV+/TB compared to HIV+/ORD ($P = 0.052$ for MS, .0001 for MPT51) but not significantly differ-

ent between HIV-TB compared to HIV−/ORD. Among US HIV+TB suspects a positive anti-MPT51 antibody response was strongly and significantly associated with TB (OR 11.0, 95%CI 2.3–51.2; $P = 0.002$).

Conclusion: These findings have implications for adjunctive use of TB serodiagnosis with these antigens in HIV+ subjects.
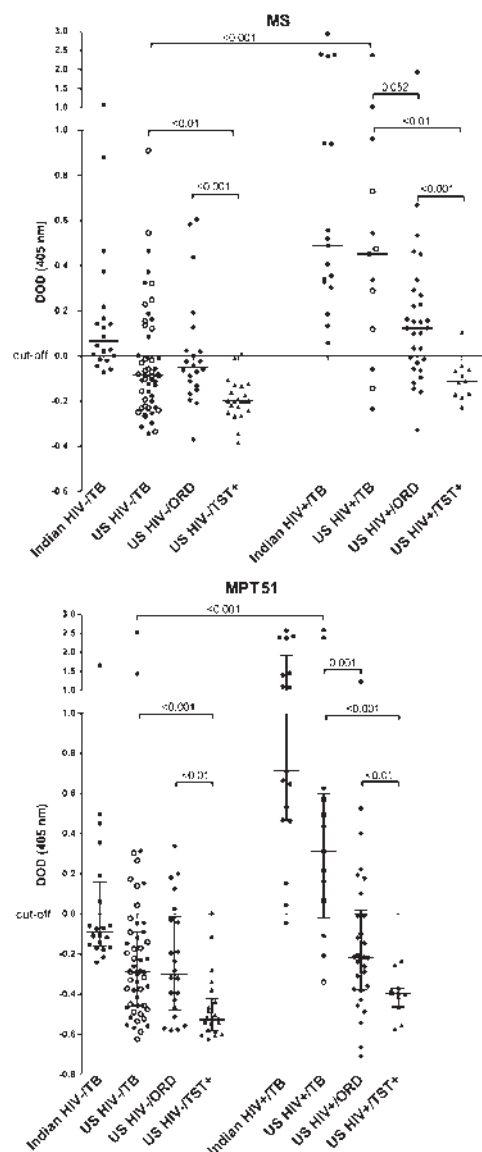
Figure Antibody reactivities to MS and MPT51 in subjects with TB, other respiratory diseases (ORD), and controls, categorized by HIV status. Cut-off values were derived from the mean OD of HIV-/TST- healthy volunteers plus 3 standard deviations; ΔOD: delta optical density after subtraction of cut-off value; ●: sputum AFB smear-positive; ○: sputum AFB smear-negative; bars show median ΔODs. Mann Whitney U test was used for two group comparison of median antibody reactivities.

PS-100575-13   Sensitivity of the T-SPOT®.TB assay following overnight storage of blood, Dar es Salaam, Tanzania

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Background: The T-SPOT®.*TB* (Oxford Immunotec Ltd, Abingdon, UK) is an interferon gamma release assay for detecting latent *Mycobacterium tuberculosis* infection (LTBI). The 8-hour processing requirement is constraining, deters use and leads to invalid results. Addition of the T-Cell Xtend™ reagent may increase allowable time to processing up to 32 hours, but has not been extensively field tested.

Methods: Smear positive TB adult patients were recruited at 2 clinics in Dar Es Salaam, Tanzania. Patients provided a medical history, 1–3 sputum samples and 1 blood sample which was transported to the laboratory under temperature controlled conditions. After overnight storage, 25 μL of T-Cell Xtend™ reagent were added per ml of blood and the sample was tested using the T-SPOT®.*TB* assay. T-SPOT.*TB* assay and culture results were compared; agreement values and the kappa statistic were calculated.

Results: 144 patients were enrolled. 58 patients were excluded because specimen transport temperatures exceeded the acceptable maximum, 19 additional patients had non-interpretable T-SPOT.*TB* assay results due to red blood cell contamination and 1 patient did not provide a sputum sample. Therefore, 66 patients with both T-SPOT.*TB* assay and culture results were available for analysis. The overall agreement between the T-SPOT.*TB* assay and culture was 95.4% (95%CI; 87.1%–99.0%) with a Kappa value of 0.548. Using positive culture as the gold standard for LTBI, the sensitivity of the T-SPOT.*TB* assay performed on blood stored overnight and processed using T-Cell Xtend™ was 96.8% (95%CI; 88.8%–99.6%).

Conclusions: When T-Cell Xtend™ reagent is added to specimens held overnight at recommended temperatures, the T-SPOT.*TB* assay is as sensitive as the standard assay.

PS-100577-13   Latent class analysis to compare the tuberculin skin test and two interferon-gamma release assays

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Background: Test characteristics of interferon gamma release assays (IGRAs) for detecting latent *Mycobacterium tuberculosis* infection (LTBI) are difficult to determine because there is no gold standard. Latent Class Analysis (LCA) is a computational method which reconciles different diagnostic tests in the ab-

sence of a gold standard. We apply LCA in a low TB incidence setting to compare sensitivity and specificity of two IGRAs and the tuberculin skin test (TST).

Methods: Three tests, TST, T-SPOT®.*TB* (Tspot), QuantiFERON-TB Gold (QFTG), were performed on adults prospectively recruited from clinical and public-health settings. TB exposure was assessed using a standardized questionnaire. The sensitivity and specificity of each test was computed using LCA.

Results: Among 362 subjects with complete data, sensitivities of TST, Tspot, and QFTG were 80% ± 8%, 94% ± 5%, and 86% ± 10% (mean ± s.e.); specificities were 89% ± 2%, 91% ± 2%, and 100% ± < 0.1%, respectively. Tspot and QFTG exhibited statistically significantly higher sensitivity than TST, $P < 0.001$ for each, but specificities were/were not significantly different for the 3 tests. For patients with prior TST, sensitivity decreased and specificity increased for all tests with increasing number of prior TSTs. For BCG-vaccinated patients, IGRA sensitivity increased and specificity was unchanged; TST sensitivity and specificity were significantly lower for this population.

Conclusions: Among all subjects in our low incidence setting, LCA suggests that IGRAs are more sensitive than TST for identifying LTBI. Our results support additional consideration of the LCA method to estimate IGRA advantage.

PS-100659-13   Patients with culture-positive active tuberculosis but negative Quantiferon test result

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Introduction: The 'QuantiFERON-TB Gold In-Tube Test' (QFT) is a diagnostic test based on the in vitro detection of interferon-gamma (IFN-γ). Both the latent and active infections with *Mycobacterium tuberculosis* are detected. The producer recommends a cut-off of 0.35 IU/ml for the test.

Methods: The QFT was performed on samples of 54 HIV negative patients during the years 2008 and 2009 all of which were previously tested positive for active tuberculosis (culture positive). As a control group we used patients with other lung diseases and no tuberculosis.

Results: We examined 45 patients with lung tuberculosis, 4 patients with lymph node tuberculosis, 3 patients with osseous tuberculosis and 2 patients with tuberculous pleurisy. The median for all patients was 3.59 IU/ml, the range was 0.00–300 IU/ml. In 11 patients the test result was <0.35 IU/ml (20% of all patients). Only in one patient with former therapy with adalimumab the result was 0.00 IU/ml, in one other

patient with lung cancer under concomitant chemotherapy it was 0.02 IU/ml. All other patients showed values of 0.07 IU/ml or above. The median age of our sample was 42 years (range: 3–90 years), in the group with a test result ⩾0.07 and <0.35 IU/ml the median age was 76 years (range: 32–81 years) and in the group testing ⩾0.35 IU/ml it was 35 years (range: 3–90 years). In the control group ($n = 60$) the median age was 61.5 years (range 2–90).

Summary: We recommend critical analysis of the cut-off value for the QFT. With a cut-off value of 0.07 IU/ml only 2/54 patients (4%) would have a false negative test result as compared to 11/54 (20%) patients using the recommended cut-off.

PS-100870-13   Risk factors for TB infection in high burden TB-HIV communities using QuantiFERON-TB Gold test

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Background: Interferon Gamma Release Assays (IGRAs), such as QuantiFERON-TB Gold In-Tube (QFT-GIT) are replacing Tuberculin Skin Test (TST) as the preferred method for diagnosis of latent TB infection in developed countries. In high burden TB-HIV settings, data on IGRAs effectiveness are limited and their future role in LTBI diagnosis remains uncertain.
Objective: To determine risk factors for TB infection in household contacts across 24 high burden TB-HIV communities in Zambia and Western Cape, South Africa, as determined by QFT-GIT.
Methods: In a prospective study between April 2007 and July 2008, 1996 household contacts of index TB patients were recruited. Notified TB patients were the point of entry into households where contacts were invited to participate. QFT-GIT, HIV and TST tests were done. A questionnaire was used to assess risk factors. QFT-GIT was performed either in central or periphery laboratories.
Results: Median age for contacts was 28 years (IQR: 20–43) and most were female ($n = 1405$, 70.7%). There were more indeterminate responses, 192 (19.1%) in the periphery than central sites, 31 (2.6%). Among contacts with determinate results, QFT-GIT was correlated with increasing age (OR for each 10 year increase: 1.15; 95%CI 1.06–1.25); HIV positive status (OR: 0.51; 95%CI 0.39–0.67) and TST (10 mm) positivity (OR: 4.3; 95%CI 3.21–5.81). Smear positive-status of the index was not significantly associated with QFT-GIT positivity among the contacts (OR: 1.25; 95%CI 0.90–1.74). Sleeping proximity to the index did not show correlation with QFT-GIT. TST showed similar correlations but agreement with QFT-GIT was poor (60.2%; kappa 0.244).
Conclusion: QFT-GIT correlates more strongly with

increasing age, HIV positivity of the contact and TST than with recent exposure measurements.

PS-101021-13   Longitudinal changes in body composition among tuberculosis patients in urban Kampala, Uganda

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Aim: Past studies have been limited to explain nutritional changes during and after tuberculosis treatment. We established the effect of wasting at diagnosis of tuberculosis on rate of change for fat-free mass (FFM), fat mass (FM), and body mass index (BMI) during and after treatment among patients in Uganda.
Methods: In a retrospective cohort study of 717 adult patients, BMI was assessed at baseline, 2, 3, 5, 6, 12, and 24 months whereas FFM and FM were evaluated at baseline, 3, 12, and 24 months.
Results: During the first three months of treatment, the gain in FFM among patients that had wasting was dramatic in men with rate of 4.55 kg/m^2 (95% confidence interval (CI) 1.26–7.83) per month; however, the gain was minimal among women with rate of 2.07 kg/m^2 (95%CI −0.74–4.88). Women that presented with wasting had a significant gain in FM at rate of 3.55 kg/m^2 (95%CI 0.40–6.70) in the first three months whereas men had a rate of 3.16 kg/m^2 (0.80–5.52). Men with wasting gained BMI at a rate of 6.45 kg/m^2 (95%CI 3.02–9.87) in the first three months whereas women, had a rate of 3.30 kg/m^2 (95%CI −0.11–6.72). There were minimal changes in body composition after month 3 and during the one year follow-up after month 12.
Conclusion: Gender but not HIV status was associated with longitudinal body composition changes during the initial phase of treatment among tuberculosis patients that presented with body wasting.

PS-100783-13   Use of IGRA in the management of a large outbreak of tuberculosis in a sixth form college in England

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In October 2008, a 16-year-old college student with a two month history of cough was diagnosed with

sputum smear-positive cavitatory pulmonary tuberculosis (TB). The college has around 2600 students and staff, including a proportion from overseas, and is situated in a low TB incidence area of England. An incident control team was convened and decided to screen by interferon gamma release assay (IGRA) all student classes having cumulative contact with the index case greater than 7 hours, in addition to family and friendship groups. In the first screening round 29/67 (43%) students tested positive, prompting further rounds of screening. In round two of classroom contacts with exposure times between 2–4 hours, 11/51 (22%) tested positive; in a third round including two large groups having less intimate contact for a briefer period (1–2 hours) 13% of 204 students tested positive. Further screening ceased at this point as positivity rates had approached guideline cut-off levels and no further contact groups were identifiable within the college setting which would distinguish their exposure risk from local background risk. During May 2009 two students outside the groups screened presented with clinical TB. Following a revised risk assessment, the whole college population was screened in addition to re-screening those previously testing indeterminate or negative. 19 more cases of active TB were diagnosed during the incident; the index case and seven of the eight cases confirmed by culture were indistinguishable on VNTR-MIRU typing. Overall, 436 cases of latent TB were diagnosed and offered treatment. Issues raised by the incident included: the role of IGRA testing in outbreaks; the apparent ease of spread from one identified infectious case; the apparent lack of a protective effect of BCG in students; and travel outside low incidence countries as an independent risk factor for TB infection.

PS-100226-13 Cost-effectiveness of IGRA for the diagnosis of latent TB infection: a review

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Aim: To review studies on the cost-effectiveness of the use of interferon-gamma release assays (IGRA) for the diagnosis of latent tuberculosis infection (LTBI).
Methods: On 9 March 2010, we searched MEDLINE and Scielo databases for studies on the cost-effectiveness of IGRAs using the terms (costs OR cost-effectiveness) AND ('interferon-gamma release assay' OR 'IGRA') AND 'latent tuberculosis'. Searches of the references lists of these articles were also carried out.
Results: A total of 15 articles were found, 10 were on the cost-effectiveness of the use of IGRAs were found, one from the list of references was added. None was performed considering high-burden country costs, 9

Author and year of publication	Population studied	Screening strategies	Perspective	Effectiveness measure	Major results
Deuffic-Burban et al, 2010	Screening adults in close contact with tuberculosis in France, with a mean age of 35	1 No screening 2 TST alone cutoff ≥ 10 mm–5 mm as alterative scenario) 3 QFT-G alone 4 TST followed by QFT-G	Health system (direct costs)	Life-years gained	TST is more expensive and less effective and QFT. QFT alone is more cost-effective than TST + QFT
Pooran et al., 2010	Screening of contacts from a UK Health System perspective	1 TST alone (cutoff > 5 mm) 2 T-SPOT.*TB* assay alone 3 TST followed by T-SPOT.*TB* assay 4 QFT-GIT alone, 5 TST followed by QFT-GIT	Health system	Number of active TB cases prevented	IGRAs, either alone or with TST, is more cost-effective, regardless of type of IGRA
Hardy et al., 2010	Immigrants from high TB incidence countries in Leeds, England	UK National Institute for Health and Clinical Excellence (NICE) guidelines	Health system	Number of LTBI cases identified	For immigrants from high-burden countries, QFT followed by chest X-ray is more cost-effective than NICE guidelines
De Perio et al., 2009	Healthcare workers from the Veteran Health Admnistration system, USA	1 TST 2 QFT-G 3 QFT- GIT	Societal	QALYs	IGRA more cost-effective than TST, irrespective of BCG vaccination status
Burgos et al., 2009	Mexican population at high-risk for developing HIV (sex workers, IV drug users and the homeless)	1 no screening 2 Targeted screening with QFT-G and HIV testing.	Health system	QALYs	In middle-income countries with high TB prevalence and escalating HIV population, targeted screening with QFT-G is cost-effective
Marra et al., 2008	Population-based database of close and casual contacts from British Columbia, Canada	1 TST alone (cutoff ≥ 5 mm) 2 QFT-G alone 3 TST + QFT-G	Health system (direct medical costs)	QALYs	QFT-G is cost-effective only in BCG-vaccinated contacts
Kowada et al, 2008	Immunocompetent close contacts of active TB patients in Japan	1 TST alone (cutoff ≥ 10) 2 QFT-G alone 3 TST + QFT-G	Societal	QALYs	QFT-G alone is the most cost-effective strategy
Oxlade et al., 2007	Immigrants at entry to Canada from countries with low, inter-mediate and high incidence of TB, close and casual contacts	1 No screening 2 Chest X-ray 3 TST (cutoff ≥ 10 mm) 4 QFT 5 TST followed by QFT	Societal	Number of active TB cases prevented	QFT-G is cost-effective in groups with high probability of disease. Use of QFT in TST-positive population only cost-effective if risk of infection unlikely
Diel et al., 2007	Epidemiological data from Switzerland	1 TST alone (cutoffs ≥ 5, 10 and 15 mm) 2 T-SPOT.*TB* alone TST + T-SPOT.*TB*	Health system (direct and indirect costs)	Number of acitve TB cases avoided and/or Life-years gained.	T-SPOT.TB alone or with TST is highly cost-effective
Diel et al., 2007a-Chest	Close contacts of active TB patients in Hamburg, Germany	1 TST (cutoff ≥ 5mm) 2 TST (cutoff ≥ 10mm) 3 QTF-G alone 4 If TST ≥ 5mm, perform QTF-G	Health system	Life-years gained	TST followed by QTF-G if ≥5 mm is the most cost-effective screening strategy

out of 10 were performed in high-income countries. The Table summarizes methods and findings of the nine articles. Screening strategies (IGRA alone, or compared to TST or sequential TST/IGRA), IGRA tests (QFT-G, QFT-GIT and T-SPOT-TB) and effectiveness measures (QALY, number of TB cases averted, number of LTBI cases identified, life-years gained) were heterogeneous. Overall, IGRA with or without TST is cost-effective, although some studies showed advantage in specific situations: BCG vaccinated, high-risk populations for LTBI or HIV, immigrants from high to low-incidence countries.
Conclusion: There are still few studies on cost-effectiveness of IGRAs, mostly in high-income low-incidence countries. Methods are heterogeneous, which

makes comparison of findings difficult. More studies are necessary before the use of IGRAs in low and middle income countries can be recommended. While detecting and treating active TB is the priority in these countries, preventive INH therapy can contribute to TB control.

DOTS EXPANSION: PROGRAMME IMPLEMENTATION/BARRIERS AND SUCCESSES

PS-100895-13   Tuberculosis case management: assessment of urban-rural factors in TB treatment outcomes in Nigeria

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Background: In an effort to reduce burden of Tuberculosis (TB) in Nigeria, TB DOT services was extended from urban to rural areas in Anambra state between 2004 to 2008. This review evaluates the results of this service expansion to rural local government areas (LGAs).
Method: A retrospective analysis of records from 6 LGAs in Anambra state was done made up of 3 urban and 3 rural LGAs. Patient profiles and treatment outcomes extracted from TB registers and treatment cards were analyzed and compared.
Result: 790 out of the total 1086 cases evaluated live in urban while 296 live in rural areas. Treatment outcome in urban compared to rural were cured (36.1% vs. 52%), treatment completed (36.1 vs. 28.0%),

	Urban	Rural	P value
Pulmonary TB	743 (94%)	291 (98%)	0.0022
Default	66 (8.3%)	20 (6.8%)	0.45
HIV positive	221 (28%)	25 (8.6%)	0.0001
Smear positive	491	228	0.0001
Cured	285/491 (58%)	154/228 (68%)	0.02
Failed	12/491 (2.4%)	3/228 (1.3%)	0.4

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defaulted (8.4% vs. 6.8%) failure (1.5% vs. 1.0%), transferred out (1.5% vs. 1.4%) unknown (13.2% vs. 2.0%). Rural LGA patients had better Treatment success rate (80.1% vs. 72.2%), better TB cure rate (68% vs. 58.0%), less HIV positive (8.6% vs. 28%), more smear positive (77.0% vs. 62.2%) more pulmonary TB (98% vs. 94.3%), more death (8.8% vs. 3.3%). No significant difference in default rate (6.8% vs. 8.4%) or disease category.
Conclusion: TB cure rate and TB treatment outcomes were better in rural compared to urban areas and supports the need and feasibility for expansion of TB DOTS services to rural areas. The higher death, more pulmonary TB in rural areas could be attributed to diagnostic challenges, poor living conditions and management of co morbidities associated with TB.

PS-100524-13   Final evaluation report on the WB/DFID TB control project in Xinjiang

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Objective: To evaluate the implementation of the World Bank Loan/DFID granted TB Control Project in Xinjiang Uygur Autonomous Region, and to provide scientific data and evidence for adjusting and formulating next TB control plan (2010–2020).
Methods: According to the forms on the final evaluation of MOH, the annual surveillance data and other materials in 96 counties of Xinjiang from 2002–2009 were collected, summarized and analyzed.
Result: The project was fully carried out in 96 counties in Xinjiang Uygur Autonomous Region, all the counties formulated and issued their respective TB Control plan (2001–2010) and established leading groups. The ability of tuberculosis prevention and treatment was reinforced, and the DOTS cover rate is 100%. The registration rate of Smear-positive of TB patients have increased from 52/100 000 to 89/100 000 from 2002 to 2005, the treatment and management of infectious TB patients for free of charge were above 98%, the cure rates of smear-positive TB patients is 91%, the cure rates of re-treatment TB patients achieved over 85%, achieve the goal of TB control plan.
Conclusion: The implementation of the World Bank Loan/DFID granted TB Control Project in Xinjiang Uygur Autonomous Region has reached the goals of the TB control project and the stage goals of China TB control plan Evaluation shows, it is necessary to do much more efforts on TB control work in Xinjiang, especially in HIV-TB, DRS-TB, migration, in order to achieve the goal of NTP.

PS-100629-13   Integration of TB information system into the national health management information system in Afghanistan

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Background: Standardized TB recording and reporting is an important component of DOTS strategy, and is necessary for effective patient and program management. NTP Afghanistan was using paper based recording and reporting system to capture minimum

program requirement. However, the system had frequent delays in reporting, incompleteness data submission and inaccuracies. In addition the data reporting was not integrated to national health information system. Computerized electronic Database was developed and piloted in six provinces. TB data collection shifted from quarterly to monthly (at provincial level) and from paper-based to computer based. The study was conducted to assess the effectiveness of integration of TB reporting into National HMIS in six pilot provinces.

Methods: The pilot was carried out in six provinces of Afghanistan, from September 2009 to March 2010. The midterm assessment was conducted in January 2010. The following variables were assessed; the speed of submission, accuracy and completeness of TB data. Monthly data from each individual health facility were collected and entered to the database.

Result: The results showed significant improvements in completeness, accuracy and speed of TB data; from 70%–85% improvement in completeness of TB data, 65%–80% speed in submission of quarterly TB data to national level and 68%–90% improvement on timeliness of reports from health facilities to provincial level.

Conclusion and recommendations: The revised TB information system has improved data management system, timely assessment of program key performance indicators, accuracy and timely submission of data. This system should be scaled-up nationwide.

PS-100761-13   TB in urban cities: implementation of urban TB project—experience from Kabul, Afghanistan

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Background: Kabul, with a population of about 5 million, has some of the low TB indicators in the country. TB case notification in 2008 was 38% compared to 73% for the country, cure rate was 54% compared with 85% for the country. The high population density, overcrowded housing, poor sanitary facilities and a higher population of IDPs which poses a particular challenge to TB control efforts. TBCAP, NTP, WHO stakeholders are implementing Urban-DOTS project in Kabul city to address the above challenges. The objective of the study was to assess the effectiveness of implementing Urban-DOTS in Kabul-city.

Methods: Kabul city has about 111 public and private health facilities, and 20% of them involved with TB control services. The implementation started on July 2009. Regular supervisory visit strengthened, 140 health staffs trained, 12 health facilities were renovated. During December 2009, an assessment was conducted and data from 3rd–4th quarters 2009

reviewed and compared with data from 3rd–4th Quarter 2008.

Results: TB service has improved in Kabul city. Seven new public TB centers established and five private hospitals involved in TB as referring centers. There was a 10% increase in the number of TB cases notified from 379 smear positive cases in 3rd–4th Quarter 2008 to 418 in 3rd–4th Quarter 2009. The cure rate improved to 66% in 2008 from 54% in 2007.
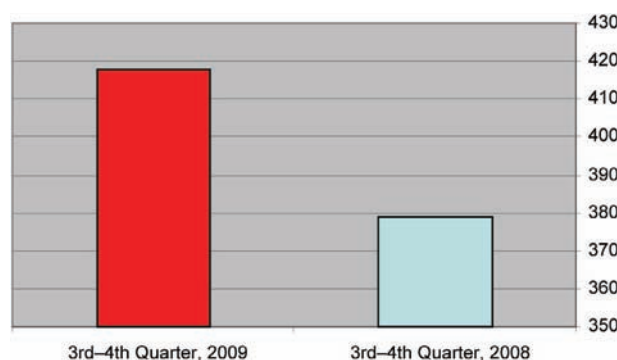
Figure   TB sputum smear positive cases notification in Kabul city.

Conclusion and recommendations: The implementation of Urban-DOTS project has improved TB services in Kabul city. This approach should be scaled-up to other urban settings with similar challenges in Afghanistan.

PS-100754-13   Implementation of community-based DOTS in four provinces of Afghanistan

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Background: Afghanistan is 22nd among high burden TB countries with estimated new sputum smear positive incidence and all type TB cases prevalence of respectively 76 and 238/100 000 population. Although, Afghanistan is detecting about 61% of TB cases, case detection is lower in remote and hard to reach areas because of inaccessibility of health facilities. Therefore, NTP/TB CAP introduced community based DOTS (CB-DOTS) in four remote provinces in May 2009 to overcome the above challenges.

Objective: To determine the contribution of CB-DOTS approach on improving TB services in four remote provinces.

Methods: The CB-DOTs was implemented in four provinces by upgrading basic health centers (BHCs) with lab services, train community health workers (CHWs), community health supervisors (CHSs) and lab technicians, orient health workers IEC materials distribution and school-bazaar events. Data was collected in October, 2009 by interviewing health workers, community health workers, TB patients and treatment supporters.

CB-DOTS map
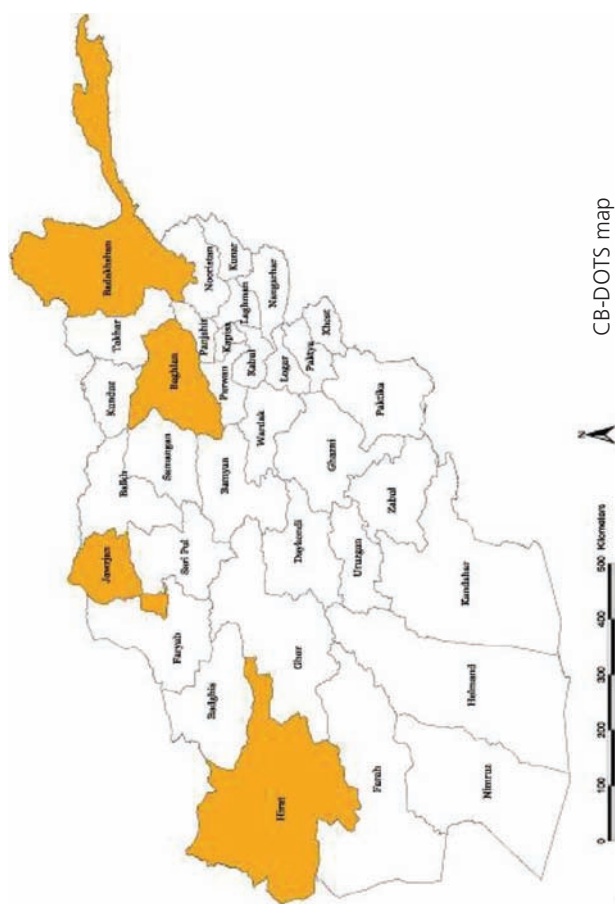
Results: Between June and September 2009, a total of 14 445 TB suspects referred to health facilities, 1407 (9.7%) turned sputum smear positives. While in 2008, suspect cases not registered/reported. CHWs identified and referred 6973 suspected TB cases, 704 (10%) turned sputum smear positives, however, in 2008, CHWs were not referred TB suspects. Currently, 358 TB patients receiving DOT either from CHWs, or treatment supporters. The adherence to treatment is approximately 98% in the intervention areas.

Conclusion and recommendations: CB-DOTS approach contributed to improved suspect management, case notification and reduced default rate. This approach should be scaled-up to other parts of the country.

PS-100977-13   Preparedness of primary health care doctors to participate in TB control in Russia

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Introduction: Effective TB detection allows reducing infection source. Low TB detection rate in Russia is often explained by primary health care doctors (PHCD) reluctance to participate in TB control. The study goal was to assess PHC doctors' perception of their role in TB control.

Methods: 206 PHCD (169 females and 31 males, median age 48) from 3 regions of Russia completed a semi-structured questionnaire on various aspects of PHC involvement in TB detection.

Results: Half of 206 PHCD had professional experience 14–29 years (median 23), but only 51% had training on TB within the last 5 years. The main referral to TB service was through the district TB doctor, 66% of PHCD had 1–5 referrals during the last year, and 53.7% met only 1–2 TB patients during the whole year. 97.5% of PHCD considered TB detection as their task. Majority of PHCD used national regulations on TB control, as well as guidelines for general practitioners. 64% of respondents followed the guidelines in full, and 28.6% partially. All PHCD considered patients coughing longer than for 2 weeks as TB suspects. Smear microscopy were used by 97.1% of doctors, and 95.5% testing results returned to the PHCD. 67% of PHCD followed up on patients referred to TB services, 71.2% received feedback from TB service on diagnosis. As constraints only 2.7% of PHCD mentioned fear of TB, 59.7% high workload, 17% absence of patients' health insurance, 21% insufficient coordination of PHC and TB services, 21% lack of knowledge on TB. 33% of respondents mentioned low health education of population, and 14% lack of incentives to comply with regulations.

Conclusion: PHCD in the studied regions of Russia had positive attitude towards their role in TB detection and followed correct procedures. Efforts must be made to optimize their workload and develop performance criteria to stimulate implementation of correct diagnostic procedures.

PS-101155-13   Improving TB services in Msambweni District using the Performance Improvement Approach

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Before Performance Improvement Approach (PIA): Low cure rate, low Anti retroviral therapy uptake (ART).

Root cause analysis: Poor District Health Management Team (DHMT) involvement in TB, Poor feedback to health workers, Lack of health workers knowledge on TB, limited laboratory services for microscopy, Lack of community involvement.

After the PIA training: The DHMT had been trained on TB and the importance of TB. The facility in charges monthly review meetings now included TB indicators. The performance of each facility was now accessed monthly. The district TB coordinator on job training to the health workers and the integrated supervision by the DHMT resulted in the health workers realizing importance of TB disease and follow up.

The health workers now owned the TB program. The facility in charges sensitized the communities around them on the signs and symptoms of TB, the importance of contact tracing and TB treatment completion. The community health workers referred patients to the health facility for screening and for sputum follow up. Sputum follow up were taken to the nearest diagnostic centers weekly after establishing sputum collecting days. Cure rate improved from 32% to 81%, HIV testing for TB patients 70% to 99.5% and the ART uptake from <1% to 50% from 1st quarter 2008 to 1st quarter 2009.

Conclusion and recommendation: PIA was able to identify root cause of the problem in a district. Involvement of the district heads is mandatory for political commitment.

PS-101301-13   An effective directly observed treatment model for controlling the tuberculosis epidemic in Kiribati

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Background and challenges to implementation: For the past five consecutive years (2003–2007), Kiribati has reported the highest annual TB case notification rate/100 000 population in the entire Western Pacific Region. In 2007, Kiribati reported 340 cases/100 000 (all forms) and 104/100 000 (sputum smear positive). In 2007, the TB case notification rate in Kiribati exceeded rates in the known high burden countries in the region such as Cambodia and Mongolia. The number of cases increased by 62% between 2000 and 2007 (from 220 to 324) and rates increased by 31% (260 to 340/100 000) indicating a rapidly increasing disease burden in the community.

Intervention: The World Health Organization and the Secretariat of the Pacific Community (SPC) declared the TB epidemic a crisis in Kiribati in 2005. A Directly Observed Treatment (DOT) model was established by the Kiribati government in 2006. Fifteen young community members were recruited, trained and established within the National TB Programme to observe TB patients swallow their TB medications and assist them to complete treatment.

Results and lessons learned: The highest recorded TB case notification rate was recorded in 2006; likely a result of increased case finding when the intervention first started. Since 2007, TB case notification rates have started to decrease; from a high of 375/100 000 in 2006 to 352/100 000 in 2008. Treatment success for sputum smear positive patients in 2006 was 90% and there were no defaulters. Treatment success has remained high since the model was introduced in 2006. In addition, no MDR-TB cases have been identified since the first case was identified in 2005.

Conclusions and key recommendations: The Kiribati DOT model of TB service delivery has made a positive impact on the TB epidemic in Kiribati. TB case notifications are starting to decrease and the treatment success rate remains high.

PS-100981-13   Implementation of DOTS Plus projects with Global Fund support and WHO technical assistance in Russia

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Objective: To evaluate the managerial challenges and first results of DOTS Plus expansion in the Russian Federation within the Global Fund (GF) Round 4 TB Control Program.

Introduction: Improvement of DR-TB management is one of the main task of GF Round 4 TB Control Program in Russia. Russian Health Care Foundation (RHCF) as GF Round 4 Principal Recipient with the technical assistance of WHO Country Office (WHO RUS) has been supporting development and implementation of regional DOTS Plus projects within GLC mechanism since 2005. 26 regional DOTS Plus projects and 4 projects in Federal Research TB Institutes were started and supported within the Program since 2005.

Results: GF Round 4 TB Control Program continued implementation of 2 Russian DOTS Plus projects (Arkhangelsk and Orel) and start 28 new DOTS Plus projects. Communication problems, lack of experience in international cooperation, complicated national regulations in drug procurement made it hardly possible for Russian regions to get drugs through GLC mechanism without external technical assistance. GF Round 4 TB Control Program resolved these problems. WHO RUS provided site selection, assistance with GLC procedures and project development. RHCF provided drug procurement, personnel training, infrastructure strengthening and social support. 7714 MDR-TB patients were approved for treatment and 6000 MDR-TB patients started treatment. First available six month interim outcome assessment reports covered 1670 MDR-TB patients and showed 62.2% of smear conversion, 19.9%—remain smear positive and default rate is 8.3%.

Conclusion: The GF Round 4 TB Control Project speeded up the expansion of DOTS Plus in Russia. Certain problem with drug supplies through GLC was the main obstacle to Program implementation. This resulted in 2 years delay in patients' enrollment. Nevertheless, the sustainable enrollment and adequate treatment have been achieved. By the 1st of March 2010 6000 MDR-TB patients were under treatment (80% of project indicator).

PS-101515-13   Implementation of the treatment supervised in the State of Rio de Janeiro, Brazil

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In 1999, the tuberculosis was declared national priority and was approved a plan national where the National Program established criteria that had included 315 cities that concentrate 70% of the cases of the illness as with priority to fortify the actions of control and to reach 100% of covering with the treatment supervised in the basic units of health. The State of Rio De Janeiro is what it presents the highest tax of incidence of tuberculosis of the country. Each year, 16 000 tuberculosis cases are notified on average. 32 priority cities concentrate 95% of the tuberculosis cases and the region metropolitan is responsible for 86% of the cases notified in the state. This study it has as objective to evaluate the process of implementation of the Treatment Supervised in the cities of Rio De Janeiro. The Program of the ERJ comes carrying through monthly meetings with the coordinators of the 92 cities of Rio De Janeiro, aiming at to evaluate the situation of the tuberculosis in the cities of the point of view epidemiologist, operational and managemental beyond considering solutions that can collaborate for the implementation of the supervised treatment of the tuberculosis. The strategy that the Program of the ERJ comes working with the cities is the decentralization of the actions in the programs of primary attention. As result the covering of treatment supervised in the state of Rio De Janeiro is increasing. In 2002 the covering of supervised treatment this tax was of 6%, with 1000 patients carrying through the supervised treatment. In the year of 2009, the covering increased for 24% in all ERJ. Of the 92 cities of state 12, they have covering between 70.0 and 99.9%, 11 cities between 50.0 and 69.9%, 25 cities of between 20.0 and 49.9% and 20 cities with covering of supervised treatment below of 19.9%.

These numbers show the trend that had increase of the number of patients in treatment supervised in the state of Rio De Janeiro.

PS-100089-13   Comparing the three approaches of hospital TB collaboration in China: a case study in four provinces

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Background: China has three approaches of hospital TB linkages: 1) The TB dispensary approach (TDA): where the TB dispensary is the sole provider of clinical and public health TB care, and general hospitals are responsible to refer TB cases to TB dispensaries; 2) the special TB hospital approach (THA), where a TB special hospital exists in TDA and also treats simple cases; and 3) the designated hospital approach (DHA), where a general hospital, called TB designated hospital, provides clinical care and the TB dispensary provides public health care.

Objective: To assess communication between hospitals and TB dispensaries, and patient experience regarding TB care, financial burden and delays under the three approaches.

Methods: Six sites were selected from four provinces to explore the in-depth information. Patient survey was conducted with 293 simple TB cases who were registered in 2007 and finished treatment by July 2008. 338 patient charts of surveyed patients were reviewed. 57 in-depths interviews were conducted with staff from TB dispensaries and hospitals.

Results: Patients experienced a high burden in the six sites, as health costs accounted for 44% of their annual household income, while 56% incurred catastrophic spending for TB treatment. In THA, 83% were hospitalised and 62% used second-line anti-TB drugs despite of being simple cases. DHA performed the best of the three approaches in terms of communication, patient hospitalisation rates, use of second-line anti-TB drugs, patient cost and delays. THA was the worst with above indicators because TB special hospital revenue heavily relied on treating TB patients. In THA and the high costs TDA site, over 80% of hospitalisation and 50% of health costs happened in the period after their TB diagnosis in the hospital and before being referred for DOTS treatment.

Conclusion: The study showed DHA may be the most promising approach in hospital TB linkage. Health system issues have to be considered.

PS-100680-13   Application of the international standards for tuberculosis care in the diagnosis of pulmonary tuberculosis

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Background: Implementation of International Standards for Tuberculosis Care (ISTC) is instrumental for effective involvement of hospitals in tuberculosis (TB) control. We assessed the application of ISTC in TB diagnosis by general practitioners (GP) and specialist physicians in general hospitals in Jakarta.

Methods: We conducted a survey targeting physicians in all (76) general hospitals in Jakarta. In each hospital we administered questionnaire to one GP and one specialist. We assessed TB diagnosis practice by

reviewing 3 medical records of the most recent patients managed by the respondents.

Results: 74 (97.37%) general hospitals in Jakarta agreed to participate in the study. 138 respondents were reviewed of which 52 (37.7%) were GPs and 86 (62.3%) were specialists. A total of 116 (84%) respondents reported that they consider patients with 2–3 weeks of cough as TB symptom. 94 (68.1%) respondents reported that they diagnose TB with acid fast bacilli (AFB) examination. 120 (87%) respondents reported performing AFB examination if chest X-ray indicates TB lesion. And 94 (68.1%) reported diagnosing AFB negative pulmonary TB in line to ISTC standard 5. We reviewed 423 medical records of which 239 (56.5%) recorded AFB examination for TB diagnosis Perceived barriers to TB diagnosis were: lack of laboratory reagents (10.8%), absence of hospital DOTS units (44.2%), lack of internal referral systems (44.8%), diagnosis cost (44.2%) and inability of patients to cough out sputum (72.3%). 90 (65.2%) respondents stated that they knew ISTC. The fraction of these respondents, who demonstrated correct knowledge of ISTC standards were: 69 (76.7%) for standard 1, 65 (72.2%) for standard 2, 79 (87.8%) for standard 4 and 45 (50%) for standard 5.

Conclusion: ISTC had not been fully applied in TB diagnosis by hospital physicians in Jakarta. Effective engagement of hospitals requires boosting knowledge of physicians regarding ISTC and addressing identified operational barriers.

PS-100037-13   The implementation effect analysis of the Hubei WB/DFID TB Control Project from January 2002 to March 2009

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Objective: To analyze the implementation effect of THE Hubei WB/DFID TB control project and provide scientific reference for sustainable development in TB control project.

Methodology: Analyze and evaluate the implementation of the project from 2002 to 2009.3 based on the final project assessment data.

Results: 1) By 2005, the county DOTS strategy coverage had reached 100%, and population coverage had reached 100%, too. 2) By the end of December 2009, a total of 262 002 active TB patients had been detected, of which 182 264 cases were smear-positive and 151 039 initial cases. The initial smear-positive TB detection rate had increased to 72.37% in 2008 from 44.34% in 2002, which has achieved the project goal (70%). 3) By the end of December 2009, a total of 160 675 smear-positive TB cases had been registered, and 151 025 cases had been cured. The cure rates of initial and retreated smear-positive TB

cases were 94.00% and 89.96%, respectively, reaching 85% of the project goal. 4) The project went on with very good cost-effectiveness, because the project's net benefits are 20.43 times the cost of treatment, obtaining a good economic efficiency. During the project period, a total of 151 025 smear positive TB cases have been cured, which can stop 1.51–2.27 million people from infecting TB and reduce 45.31–75.51 million of TB patients. It has effectively reduced the TB incidence and achieved good social effects. 5) Since the project started, more than 10 operational researches have been carried out. Two researches have received Hubei significant scientific and technological achievement appraisal, and one has got a third scientific and technological progress prize. It has improved the capacity, and effectively promoted the implementation of TB control program.

Conclusion: This project was well implemented in our province with both good economic and social benefits. DOTS coverage, and the detection and cure rate of sputum-positive patients improved.

PS-100224-13   TB control activities in conflict-ridden Ituri in Democratic Republic of Congo

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Background: In 2006, NTP assessed performance of Provincial Coordination Units (PCU) in the whole nation and identified 5 underachieving PCUs. Among them, Province Oriental East (POE) in Ituri district in north-eastern region, which faced the ethnic conflict (2001–2004) and under insecure situation even after the ceasefire, failed in improving the performance.

Objectives: To identify influential factors associated with conflict in order to protect the people for TB.

Methods: We compared the POE data with Bas Congo West (BCW), PCU in relatively peaceful region. Aggregated available data were obtained from POE and BCW archives for the past ten years: 3 years pre-conflict, 4 years conflict and 3 years post-conflict phases. The major compared indices were detection rate and treatment outcomes of new smear positive (SS+) and relapse cases.

Results: Of new SS+, both case detection and cured rates in BCW were significantly higher than that in POE ($P < 0.0001$ and $P < 0.0001$, respectively). Default rate was significantly higher in POE ($P < 0.0001$) than BCW. In POE, 32.1% of patients were not evaluated in 2001, and about 112% of patients were evaluated in 2004. For relapse cases, cured rate of POE was remained less than 60% with high fluctuations. Death, default and failed rates were still higher in

POE than BCW. TB-HIV was reported by many NGO's as life threatening conditions for people in Ituri.

Conclusion: The magnitude of the problems influenced on the default rate was great in POE, which seems due to destruction of health facilities and displacing population led by the conflict. With paying more attention on MDR-TB emergence in Ituri, we recommend: 1) Promoting public education by utilizing former TB patients; 2) Launching alternative DOTS strategy for conflict area; 3) Establishing better surveillance system in collaboration with humanitarian agencies; and 4) Providing care for co-infected TB-HIV with active case detection activities.

PS-101148-13   Community TB in Likoni District

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Objective: To evaluate the impact of the community in TB care.

Method: A retrospective cross-sectional analysis was performed on routine TB data for the period 1 January 2006 to 30 December 2007 in each of the facilities in Likoni Zone. Cases from the GOK facilities were compared with those from community based treatment centers.

Results: In 2006 there were 2 community treatment centers with 91 (12%) out of 744 patient registered. The treatment success rate for the community was 83% compared to 75% in government (GOK) facilities, giving a treatment success rate of 76% in Likoni District in 2006.

Scaling up of community treatment center took place in 2007 from 2 to 5 centers. The community based treatment centers took care of 205 (44%) out of 873 patients registered in 2007. The treatment success rate for the community was 89% and GOK 81% in that year giving a treatment success rate of 86%.

Conclusion: The increase in number of treatment centers from 2 to 5 in the year 2006 to 2007 increased the number of patients in community treatment centers from 91 to 205 giving a treatment success rate improvement from 68% in 2006 to 89% in 2007. There is need for more community engagement in TB care. Acceptance of the community approach by the healthcare workers, community volunteers, patients and their DOTS supporters is mandatory for TB care.

PS-101387-13   Strategy for TB control in Haitian migrants in the Dominican Republic, 2009–2010

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Introduction: As part of agreements to control TB in the Island of Hispaniola, in 2005 it signed an agreement committing the health authorities of the Dominican Republic and Haiti in designing strategies for the detection and monitoring of TB cases in both countries. This binational plan has involved the collaboration of international agencies, is being implemented in the Dominican Republic with tangible results in 2009 is integrated into these efforts, the TB project funded by the Global Fund.

Objectives: To support the actions of the control program of tuberculosis to prevent and treat TB in the case of Haitian migrants. Increase awareness about TB in Haitians living in the country and reduce the stigma and discrimination associated with TB in this population.

Methods: Development plan for prevention and control of TB in vulnerable populations, training of health personnel, patient card design, training of promoters of Haitian nationality and monitoring of TB cases.

Results: With support from the Global Fund, charged designation migrants, 93 managers trained PCT, 3175 cards distributed, 140 Haitians trained promoters, 8 TB patients referred (4 dropouts, 3 in Haiti, 1 in Dominican jail), home visits to patients in treatment, design materials in Creole.

Conclusions: The coordinated efforts between nations of different languages and cultures are possible when you have a common goal. Of continuing efforts to meet the goals of the plan, not only in border communities but across the country.

PS-101522-13   Process of development of supervised treatment in the State of Rio de Janeiro, Brazil, 2009

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In 2004, tuberculosis was declared a national priority and in this year was approved a national plan for the period of 2004–2007. The National Program for Control of Tuberculosis defined the 315 municipalities that concentrate 70% of cases of disease in the country, as a priority to strengthen control actions and achieve 100% coverage with supervised treatment in primary health care. The State of Rio de Janeiro is the one with the highest incidence rate of tuberculosis in the country. Each year, is reported an average of 16 000 cases of tuberculosis. The 32 priority municipalities in Rio de Janeiro concentrate 95% of cases of tuberculosis and the metropolitan region is responsible for 86% of reported cases in the state. The Program of Tuberculosis Control of the State Health Secretariat of Rio de Janeiro (PCT-SESDEC-RJ) has been conducting meetings with the coordinators of the 92 municipalities of the state. The aim of these meetings is to evaluate the tuberculosis situation in the districts under epidemiological and operational point of view and to propose solutions that can contribute to the

implementation of the supervised treatment of tuberculosis. The strategy that the PCT-SESDEC/RJ has been working with the municipalities is the decentralization of the PCT and the inclusion of these shares in Primary Care Programs exists. As a result the coverage of supervised treatment in the state of Rio de Janeiro is increasing. In 2002 the coverage of supervised treatment was 6%, with 1000 patients completing the treatment and supervision treatment; in 2009 increase to a coverage of 24% across the state of Rio de Janeiro. From 92 municipalities, 12 have coverage from 70.0 to 99.9%, 11 municipalities from 50.0 to 69.9%, 25 municipalities from 20.0 to 49.9% and 20 municipalities coverage of supervised treatment below 19.9%. These figures show the trend of increasing number of patients under supervised treatment in the state of Rio de Janeiro.

PS-100587-13 Pilot study of directly observed therapy for pulmonary tuberculosis in Eastern Taiwan

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Objective: To evaluate the efficacy and feasibility of a 62-dose, four-drug, 6-month, twice-weekly regimen administered by directly observed therapy for the treatment of pulmonary tuberculosis.
Design: A single arm, open label, non-blinded operational research, with 24-month post-treatment follow-up.
Methods: From January 2004 through December 2006, a total of 116 patients with suspected or confirmed pulmonary tuberculosis were enrolled; 32 of these patients were excluded from the analysis because of drug resistance, negative culture, self withdraw, or adverse drug reactions. Isoniazid, rifampin, pyrazinamide, and ethambutol were administered daily for 2 weeks, followed by twice weekly in higher doses for 6 weeks. Thereafter, isoniazid, ethambutol, and rifampin were administered twice weekly for 18 weeks. Treatment was directly observed by nurses or outreach workers.
Results: Of the 84 evaluable patients, 75 (89.3%) patients were considered treatment success, 3 (3.6%) transferred out, 5 (6.0%) failed and 1 (1.2%) died. Three patients had recurrences of pulmonary tuberculosis, and the recurrences were 4, 6, and 15 months after the completion of therapy. Six patients (6.7%) had severe adverse drug reactions and had their regimen modified.
Conclusions: This four-drug, largely twice-weekly pulmonary tuberculosis treatment regimen is efficacious and relatively nontoxic, with a higher treatment success rate and a lower death rate compared to traditional regimens. It simplifies treatment greatly and facilitates the execution of directly observed therapy. However, acquired resistance was a concern.

PS-100610-13 The economic impact of tuberculosis treatment on Rio de Janeiro's healthcare system

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Aim: Several studies have shown that directly observed treatment (DOT), one of the components of the DOT strategy (DOTS), is effective in the treatment of tuberculosis, but has higher costs. This study estimates the cost-effectiveness of DOT compared to the self-administered treatment (SAT) strategy in Rio de Janeiro, using the health system perspective.
Methods: Costs from 21 healthcare units were collected, with information on personnel gathered from the municipal health secretariat. Present DOT in Rio includes supervision 3×/week in the intensive phase and twice/week in the continuation phase. The effectiveness measure was cure/treatment completion rate (C-TC). The Incremental Cost-Effectiveness Ratio (ICER) for each C-TC was calculated.
Results: The ICER of the DOT compared to the SAT was US$2020 per C-TC. The cost-effectiveness ratio (CER) for DOT and SAT was 279 and 82 respectively. The health system cost per patient for the DOT was US$220.05 and US$58.45 for the SAT strategy. Considering the annual incidence of 15 000 cases in Rio, the DOT strategy accounted for an extra US$3 000 000.
Conclusion: The ICER for the health care system with the adpoted supervised treatment strategy is high (more than US$2000 per completed treatment). Although the strategy was more effective (8%), the supervision is 27% more expensive than the self-administered strategy. Several studies have evaluated different supervision strategies (community DOT, fam-

Table Incremental cost-effectiveness ratio (ICER) for the health system of DOT compared to SAT for each C-TC

Strategy	Cost [C] (US$)	Effective-ness (C-TC) [E]	[C/E] (US$/ C-TC)	ICER [△C/△E]
SAT (n = 103)	US$58.45	0.71	82	0
DOT (n = 115)	US$220.05	0.79	279	R$2,020

Dollar Exchange Rate: R$1.77–Source: Central Bank of Brazil–March 11, 2010

ily supervision). Some of these studies have shown these strategies to be as effective as DOT, and might be considered as possible alternatives in places where resources are scarce. These new strategies need to be evaluted and their cost-effectiveness measured.

PS-100665-13 La integración entre el programa de control de la tuberculosis y el programa de salud de la familia

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Una pesquisa evaluativa fue realizada en el municipio de Niterói, región metropolitana de Rio de Janeiro, con el objeto de conocer la integración y el grado de implantación de los Programas de Control de Endemias en dos distintos modelos de atención básica: el Programa de Salud de la Familia (PSF) y la atención en unidades de salud de modelo tradicional. Entre los programas, las acciones de control de la tuberculosis fueron elegidas como la condición del marcador debido a las altas tasas de incidencia. Fueron desarrollados el modelo lógico del Programa de Control de la Tuberculosis (PCT) integrado al PSF y el modelo teórico de evaluación. Para operacionalizar los modelos de evaluación, se utilizó el estudio de caso. La unidad de análisis elegida fue la Fundación Municipal de Salud de Niterói, y para la coleta de las evidencias fueron seleccionadas dos policlínicas y un módulo del PSF que diagnostican, acompañan y tratan pacientes acometidos de tuberculosis. Los resultados enseñan que: El modelo desarrollado para la evaluación fue adecuado para contestar a las preguntas evaluativas, con validad interna y que puede reproducirse. El municipio está aumentando la inversión financiera en salud y fue el pionero en la implantación del PSF; las coordinaciones del PSF y del PCT son compuestas por profesionales cualificados y expertos, pero con poca participación en las decisiones sobre la utilización de los recursos; la integración entre los programas se da de manera no sistemática y, en las unidades de salud estudiadas, la implantación del PCT es parcial. Los resultados de tratamiento con la utilización de tratamiento directamente observado (TDO) fueron excelentes, con tasas de cura de 96%, 2% de abandono y 2% de óbitos. Sin embargo, hay una proporción reducida de pacientes bajo TDO, la mayor parte de ellos acompañados por el PSF.

PS-100692-13 TB patient referral mechanism between tertiary care hospitals and primary health care, Punjab, Pakistan

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Background: Pakistan is high burden disease country. DOTS has been implemented in public sector and now expanding towards private sector and tertiary care hospitals (TC). There is no effective referral transfer mechanism between TC and Primary health Care (PHC) level. A study was designed to see feasibility of referral mechanism from TC to PHC.
Objective: To assess the feasibility of the Ext-HDL Guidelines for implementing TB patient referral/transfer (T/R) mechanism.
Methods: Study design; Descriptive, observational, Referral mechanism; Sending BMU fill TB T/R, color coded form in quadruplicate for, the sending, receiving BMU, patient and DTC-receiving BMU. maintained electronic Register. Receiving BMU send Acknowledgement and Outcome feedback to sending BMU, quarterly HDL Reports. Study period one year (2009). Study Area; 3 TC hospitals; Gulab Devi, Mayo and Sir Ganga Ram Hospitals Lahore and 526 BMUs in PHC Punjab. Study Subjects; TB Patients Referred/Transferred out from TC hospitals. Data was collected from referral register and quarterly HDL reports. Measuring indicators; Access rate, Outcome feedback rate.
Results: 523 patients were referred and 75 transferred out from TC to PHC. 219 patients were accessed to the destination (excess rate 37%). Method of confirmation was by mail in 39, DTC in 54, and phone in 126. For qualitative findings, 419 patients, unconfirmed by mail were contacted on phone. 71 had wrong phone number, 165 did not attend phone, 4 died. Only 179 were interviewed. Out of these, 144 confirmed their access to planned BMU and 35 were not accessed. $P = 0.000$. Out of 35, 29 accessed to BMU other than planned BMU Reason for non ac-
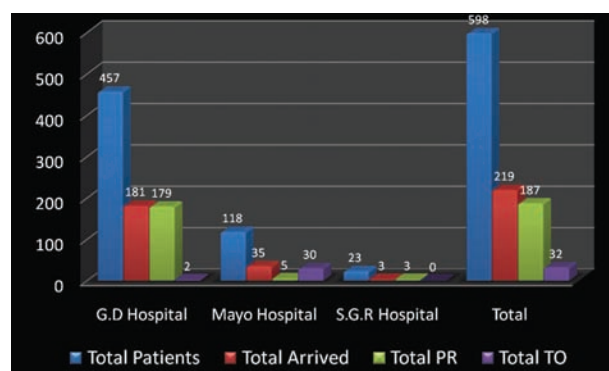
Figure Status of patients referred and transferred out.

cessing was long distance of patient home and lack of trust on receiving BMU.

Conclusion: Access rate by mail was low, but it was significantly high (80%) amongst the patients who were contacted by phone. Recommendation; Confirmation of access should be done by both mail and phone, with Referral to appropriate BMUs.

PS-101408-13   A post market surveillance of anti-tuberculosis medicines in Kenya, 2009

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Background: The number of TB cases notified in Kenya has increased tenfold since 1990 while the TB incidence of infectious forms TB increased from 32 per 100 000 in 1990 to 108 per 100 000 in the year 2007. Despite significant progress in TB control, it is important that Anti-TB drugs should be safe, efficacious and of high quality according to DOTS strategy. In Kenya there are limited reports available on the assessment of quality of fixed dose combinations for anti-TB drugs on the Kenyan market and in particular the public health facilities.

Methods: A cross sectional survey was carried out and a total of 77 TB treatment sites across the country sampled, questionnaires, sample collection and interviews were carried out.

Results: 78% of the sites had appropriate storage conditions while percentage humidity ranged from 33–62%, there was however significant differences in humidity across the sites ($P < 0.05$). From the laboratory results of the 120 product sample analysed, 10 failed to comply with one or more of the test parameters, representing 8.3% failure rate. All the non-compliant products were 2 component FDC samples with RH combination accounting for 80% of non-compliance and the EH combination accounting for the remaining 20% of failures.

Conclusions and recommendations: The results indicate that the samples analyzed were generally of good quality with only an overall failure rate of 8.3% and follow up should be made on the failed batches for corrective action. There should thus be regularly post marketing surveillance and batch by batch testing in all sectors.

DOTS EXPANSION: TB CASE DETECTION

PS-100451-13   Improvement of chest radiological diagnosis of smear-negative tuberculosis in Cambodia

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Introduction: To improve chest radiological diagnosis of smear-negative tuberculosis (TB), the specific training was conducted in late 2007, regular supervision was done since early 2008 in which chest X-ray films were reviewed since 2009. The project covered ten rural provinces with population of 6 867 958 (51.3% of the country), served by 32 peripheral chest radiography facilities (out of 59 nationwide).

Method: Smear-negative TB suspects were referred from health centers to district or provincial hospitals for chest X-ray. Diagnosis of smear-negative TB was done by local technical working group (TWG), and set up at the hospital the chest X-ray films were further reviewed by the Cambodia National TB Program (NTP). Sensitivity and specificity of diagnosis were calculated with the decision of NTP as gold standard. Data were collected from 1st quarter to 4th quarter, 2009.

Results: The numbers of chest X-ray films examined both by TWG and NTP were 733, 894, 937 and 961 from the first to fourth quarters of 2009, respectively. The specificity of the diagnosis of 'active TB' against 'normal' or 'other respiratory disease' combined on chest X-ray done by TWG compared with that by NTP team improved: it was 77.7%, 90.9%, 87.8% and 92.0% in first to fourth quarters of 2009, respectively. The sensitivity of the diagnosis has remained with a range of 93.5 to 96.4% during the same period.

Conclusion: This study showed great improvement of chest radiological diagnosis of smear-negative tuberculosis probably due to training and regular supervision.

PS-100630-13   Small initiative, wider replication: experience from FIDELIS project in Afghanistan

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Background: For the first time ever, BRAC Afghanistan was awarded for the FIDELIS project in Afghanistan with the support of The Union. The Phase 1 started in Jan 2006, covering 5 provinces and 34 districts, ended in Dec 2006. And Phase 2 was an 18 months project started in July 2008, covering 7 provinces and 52 districts, ended in Dec 2009 with two months no cost extension up to Feb 2010.

Project approach: The aim of this project was to control and treat Tuberculosis through Community Health Workers (CHW) at the community level and increase access to diagnostic services through establishing Laboratory at Basic Health Centers and conducting Mobile Diagnostic services. CHW was paid performance incentives i.e. $1 for detecting smear positive TB case and $3 for completing course of DOT for TB patient.

Result: There was a steady increase in case detection in project implementing areas. The CDR was 18.6% in 2005 before implementing the project. By end of 2006, CDR increased to 60% and in 2007 to70.3%. This project was only implemented in 7 out of 34 provinces of Afghanistan. Based on the good result of the project, it was replicated to another 4 provinces with the support of USAID through TB CAP project. Now, the similar approach has been incorporated in Global Fund Round 8 proposal and is implemented at national level.

PS-100673-13   Systematic approach for improving TB case detection: a novel approach from Ghana

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Background: One of the key challenges facing National TB Programs (NTPs) in Africa is the low TB case detection. Ghana is among the countries with low TB case detection rates. In 2007, the World Health Organization (WHO) estimated that only about 26% TB cases were detected in the country. Innovating strategies for improving TB case detection rate in Ghana are urgently required.

Intervention: In April 2009, a situational analysis of TB case detection practices in health facilities was conducted. One of the weaknesses identified was lack of tools to enable health workers identify and diagnose TB patients. Through a participatory approach SOPs for TB case detection were developed. The SOPs are currently being implemented in Upper West Region which had a TB case detection rate of 11% in 2008. Hospital personnel from all key departments which included antiretroviral therapy (ART) clinics from all the 10 main hospitals were trained in the use of the SOPs.

Results: During the first quarter of the use of the SOPs 100 TB cases were diagnosed and put on TB treatment. This was a 69% increase of TB case detected as compared with the 59 cases detected per quarter during the year 2008, which was used as baseline.

Conclusion and recommendations: The use of SOPs

for TB case detection has increased the index of suspicion for a TB suspect. However, regular in-service training should be conducted as the region has a high rate of attrition of staff.

PS-100829-13   External quality assessment of smear microscopy in DR Congo

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Introduction: As part of DOTS programs, AFB detection using microscopy is the technique recommended for both TB diagnosis and patients monitoring during treatment. In 2006, the NTP in collaboration with the UNION did implement new guidelines for External Quality Assessment (EQA) across the TB microscopy centers that diagnose about 100 000 TB cases each year. The EQA method is done by blinded rechecking of 48 slides per year and per center.

Aim: To assess the performance of diagnosis in the TB microscopy centers.

Methods: We perform a retrospective analysis of reports coming from all the 24 provincial laboratories within the country. The outcomes of interest were: EQA coverage, the positivity rate, sensitivity and positive predictive value (PPV) for the entire network of microscopy laboratories working with the NTP DR Congo.

Results: In 2007, a total of 1177 (95%) among 1235 operational TB microscopy centers did participate to the EQA. The positivity rate was 17%. The sensitivity was 85% and the PPV was 94% for the entire network of microscopy laboratories in NTP DR Congo.

Conclusion: The performance of smear microscopy diagnosis in the TB laboratories network of NTP DR Congo seems good. To achieve Tuberculosis global control, these performances of smear microscopy should be maintained overtime.

PS-100956-13   Hospitalization policy for smear-positive TB patients to increase sputum conversion rates in lower Northern Thailand

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Aim: To assess patient satisfaction and a treatment success rate of patients being hospitalized for two weeks according to the national TB policy.

Method: The quasi experimental research (one group Pretest Posttest design) was conducted during May July 2009 in 5 provinces in lower northern part of Thailand. Participants were 78 TB patients and 41 health personnel from TB clinic, laboratory, administrators. All participants were interviewed by an instructed questionnaire. TB register was also reviewed.

Results: The duration of hospitalization of smear-positive TB patients were 8–14 days (47.4%), 15–21 days (30.8%) and 1–7 days (20.5%). Knowledge, attitude and practice between pre-test and post-test were significantly different ($P < 0.001$, < 0.001 and 0.019). TB patient satisfaction about the hospitalization policy was 45.1% in high level, 39.6% in medium level and 15.3% in low level. It was found that sputum conversion rate of hospitalized patients (87.2%) was significantly higher than those (73.6%) without the hospitalization ($P = 0.001$). However, health staff complained about the workload and was worried about the TB transmission in the hospitals.

Conclusion: The hospitalization policy for smear-positive TB patients could strengthen the TB control program in terms of patient satisfaction and sputum conversion rates. However, infection control strategy and workload are critical for implementing the hospitalization policy.

PS-101146-13   Results from the implementation of external quality assessment for smear microscopy in Tajikistan

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Background: Blinded rechecking method for EQA of smear microscopy in Tajikistan was implemented gradually, starting in 2005 with participation of 44, out of 97 functioning laboratories. By the end of 2009, total number of 92 laboratories (95%) participated in the EQA program.

Objective: To evaluate the effectiveness of the implemented method for EQA.

Method: The estimation of the representative sample size for rechecking was based on LQAS method and the slides were randomly selected from all slides examined during the year. Rechecking was organized on quarterly basis with involvement of National Reference laboratory (NRL) and five intermediate level laboratories. Evaluation criteria were: sensitivity compared to controller 80% and acceptable error 1 or 0, depending of the size of rechecking sample.

Table   Laboratories participating in EQA and results by year of implementation

	Participating laboratories		Laboratories with satisfactory results	
Year	*n*	*%*	*n*	*%*
2005	44	45	—	—
2006	56	57	20	36
2007	79	81	51	64
2008	91	94	57	63
2009	92	95	63	68

Results: During the examined period the results of EQA present the tendency of improvement in quality of smear microscopy. The improvement was also found in terms of the quality of smear preparation, from 39% in 2005 to 66% in 2009.

Conclusion: Implementation of blinded rechecking method for EQA in Tajikistan helped the NRL to detect the problems in functioning of smear microscopy network and take remedial actions in a timely manner. The implementation of this method significantly improved the quality of smear microscopy.

PS-101166-13   Challenges of implementing external quality assessment and supervision for microscopy in Malawi

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Aim: To address challenges in improving the quality of rural TB microscopy services in Malawi.

Methods: Twelve Ministry of Heath TB smear microscopy sites in Zomba and Mangochi districts, supported by USAID's Tuberculosis Control Assistance Program, were targeted to improve microscopy, and implementation of supervisory and External Quality Assurance (EQA) systems. Baseline assessments were conducted to identify barriers to delivering quality microscopy services. Interventions to improve quality included physical renovation of the laboratories, provision of Global Drug Facility (GDF) Laboratory Kits, re-training of microscopists, the introduction of new laboratory registers and mentoring of laboratory supervisors. Quarterly supervisory visits and EQA, using blinded rechecking and the Lot Quality Assurance System were introduced. Feedback was provided to each laboratory on their quality improvement.

Results: The major constraints affecting the quality of microscopy results were; poor laboratory organization and practice, unsafe premises, long turn-around time for results, low staff morale, high staff turnover, poor storage and transportation of specimens, inadequate safety measures, including waste disposal, and poor record keeping. After these had been addressed, the overall performance score (i.e. concordance of results in EQA) for each of the four quarters in 2009, was 98.8% for Mangochi district and 98.6% for Zomba district. The turnaround time for results dropped from 3 or 4 weeks to 24–72 hours.

Conclusion and recommendations: Working in a safe conducive laboratory environment with well equipped, uninterrupted quality assured supplies motivates microscopists to provide high quality results. Regular on-site mentoring and supportive supervision facilitates the provision of quality assured, timely and reliable results, required for improved case detection of TB.

PS-101211-13 Evaluation of quality microscopy service using EQA performance on reading and smear preparation

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Background: A newly developed External Quality Assessment (EQA) System for AFB Microscopy employing Lot Quality Assurance Sampling (LQAS) was introduced into the NTP by the Department of Health in 2004. The new EQA System was first implemented in 19 provinces/cities nationwide as pilot sites. One QA center in each site has been established to oversee its implementation.

Objective: To evaluate the performance of all microscopy centers (MC) of the pilot sites in the Philippines by assessing their EQA results on blinded rechecking and smear preparation quality check, from 2005 to 2007.

Method: Data analysis of 361 MC from 19 pilot sites was carried out. The standard targets of no major error for blinded rechecking and at least 90% proportion of good quality smears for each assessment point, which are based on National EQA Manual, were used to evaluate the performance of MC.

Results: Decreasing trend in the proportion of Major Errors (HFP and HFN) has been observed after the first year of the new EQA implementation. However, three among the six assessment points have not reached the 90% proportion of good quality smears. Collection of specimen may be a contributing factor in poor specimen quality, smear thickness and evenness. EQA results also indicated an increasing number of MC having no major errors from 2005 to 2007.

Conclusion: The quality of sputum smear microscopy service in the pilot areas is generally good based on the assessment of EQA results. The present good quality microscopy services must be maintained if not further improved. Continuing efforts to improve the laboratory services through EQA activities and programmatic initiatives must be sustained in order to maintain or further strengthen the good performance of MC nationwide.

PS-101392-13 Evaluation of EQA using blinded rechecking of acid-fast bacilli smear microsopy in Sudan, 2009

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Setting: 226 Tuberculosis management units (TBMUs) distributed into 12 northern states in Sudan applying the EQA system.

Objective: To assess the quality of acid fast bacilli (AFB) microscopy services using blinded rechecking

system in order to generate useful information to improve the overall performance of the system.

Methods: Routine slides which stored for the 3rd quarter were collected with their results. Then they were rechecked at both state and central levels (1st controller). The discordant were identified and rechecked at central level by other technician (2nd controller). Re-staining of slides was done at NRL for discordant slides and all other slides which reread before and after stain. The lab supervision check list was used for assessing the available laboratory resources.

Results: Evaluation of TBMUs and state quality control lab (1st controller) in the northern states found that the agreement rate was 95.5% and 98.1% respectively; while the FP rates were 13.1% and 5.7% compare to 1.9% and 1.0% for FN rate respectively. According to the errors discovered, it was found that 58% of labs out of the lab visited had acceptable performance while the rest (42%) with unacceptable performance. Regarding work load it was found that 19% of labs had adequate number of examinations per day and 21% had less than 1 examination per day while only 1% appeared high work load per day.

Conclusions: The quality of most laboratories in TBMUs was not reached the satisfactory levels. Presences of many FP rates due to lack of standard training curriculum, poor condition of the microscope, poor reagents preparation and other unknown reasons need to be investigated.

Recommendations: NTP and NRL need to develop a high quality standardized training course for AFB microscopy diagnosis.

PS-101407-13 Addressing challenges in preparing the TB central laboratory, Malawi, for an MDR-TB survey

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Background and challenges to implementation: In 2008 the CRL had problems with the quality of results due to operational difficulties. The laboratory was also operating at Bio-Safety Level (BSL)-2 and with no documented safety procedures. These issues needed to be addressed before an MDR survey could start.

Intervention: Technical assistance was provided by a partnership of local and international organisations focussed on preparing for the MDR survey. This helped to guide the process of refurbishment to BSL-3 and to build the capacity of local laboratory and National TB Programme (NTP) staff in preparation for the survey focusing on the CRL management processes. The laboratory was upgraded to BSL-3 using

regional contractors taking a year to complete. CRL and NTP systems were reviewed to improve procedures, transport, communication, safety and human resource management. Support for these changes from staff already engaged in the CRL and NTP was deemed critical and large amounts of time were devoted to ensuring this was obtained.

Results: Early results indicate an improvement in key laboratory quality indicators (see Table). CRL staff have demonstrated greater acceptance and adherence to quality assurance, safety procedures and new technologies. These results suggest that capacity building of CRL staff through consistent support with the clear medium-term aim of completing a national MDR survey could lead to sustainable improvement, even in resource constrained environments.

Year	Samples processed	Contamination rate	Smear positive isolation rate	Samples reaching CRL within 4 days of collection
2008	1736	37%	70%	0%
2009	Laboratory closed			
2010 (partial)	229	1%	94% (4 weeks of culture)	76%

Key recommendations: There are two key challenges now: sustaining quality as the MDR survey gathers pace while starting to focus on the longer term sustainability of core CRL functions. To promote ownership, external assistance should be scaled back as the survey continues so that improvements made through the survey can feed into routine practice. This approach could be considered in other resource poor countries preparing for DR surveys as a catalyst to improving diagnostics services.

PS-100010-13   Chest radiography accuracy in screening pulmonary tuberculosis in immigrants from an endemic country

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Background: The accuracy of chest radiography (CXR) in diagnosing and screening pulmonary tuberculosis (PTB) is debatable and its costs are relatively high. This retrospective study aims to determine the accuracy of CXR in detecting active-PTB or old-healed tuberculosis (OHTB).

Methods: All Ethiopian immigrants to Israel between 2001 and 2005 were radiographed before migration. Immigrants whose CXR demonstrated PTB or OHTB were evaluated, treated and followed-up for one year after arrival in Israel.

Results: CXR was performed to 13379 immigrants. Changes suggesting PTB were identified in 150 (1.2%). Of those, 46 were diagnosed with active-PTB. Sensitivity, specificity and positive predictive value (PPV) of a CXR suggesting PTB were 80.1%, 99.2% and 31%, respectively. Post-test odds calculations demonstrate that Ethiopian immigrant whose CXR demonstrates changes suggestive of PTB has 40 times likely to be diagnosed with PTB than an immigrant whose CXR is unremarkable. Changes suggesting OHTB were identified in 257 (1.9%) immigrants. Of those, 15 (5.8%) developed active-PTB within one-year following arrival. Sensitively, specificity and PPV of CR suggestive of OHTB were 17.2%, 98.1% and 5.8%, respectively, when active-PTB during the first year was the end-point. In this study, 291 CR were required to detect one active-PTB patient, in the cost of US$5802.

Conclusions: CXR is a relatively sensitive and cost-saving tool for mass screening for PTB among immigrants originating in a high-tuberculosis burden country. CXR is also beneficial in detecting OHTB in immigrants who are at a higher risk for developing active-PTB.

PS-101278-13   Using a community approach to improve the TB case detection rate, Mpigi District, Uganda, 2008–2009

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Background: Mpigi district has 22 TB diagnostic and treatment units (DTUs) and over 300 teams of community health workers, called village health teams (VHTs). Despite the efforts in TB control, TB case detection rate (CDR) remained below 70% for years. Challenges: insufficient distribution of DTUs; demotivated laboratory staff; TB microscopy being a long, laborious process; staff fear of TB infection; and preference for radiology over microscopy in diagnosing TB.

Interventions put in place with financial and technical support:

Community sensitisation to access TB services: Starting third quarter 2008, VHTs were sensitised on determining TB suspects and charged with the responsibility of sending them to DTUs. Children from 208 schools were sensitised and given messages about TB prevention for their families. Furthermore, four community drama groups gave performances addressing TB prevention.

Filling programmatic gaps to increase access to laboratory services:

Of the 15 TB microscopists needed, 11 were trained, 5 of 10 microscopes needed were provided and TB microscopy was started in 3 remaining facilities designated as DTUs. An Intensified Case Finding Form was implemented and training emphasized use microscopy rather than radiographs to diagnose pulmonary TB.

Results: Despite the interventions in Q3 2008, a national stock out of anti-TB drugs from Q4 2008 Q2 2009 overrode the effects of the support. It was only from Q3 2009 that the support led to an increase in examined TB suspects and the CDR.

	2008 Before support				2009 With support			
	Q1	Q2	Q3	Q4*	Q1*	Q2*	Q3	Q4
Examined, *n*	448	620	588	462	497	419	571	670
CDR, %	66.3	76.5	64.3	81.9	66.8	52.8	72.8	78.8

* National stock out of anti-TB drugs led to decreased services.

Conclusions and recommendations: Community approaches not only sensitise communities about TB, but are also useful in referring patients into the health care system. For CDR to improve, financial and technical support needs to be coordinated with provision of and offered at the same time as drugs. The approach is recommended for places with similar challenges.

PS-100840-13 Early identification strategies of potential tuberculosis suspects in communities of Western Kenya

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Background: The intent of Intensified Case Finding (ICF) is to detect cases of TB earlier than traditionally occurs with passive case detection. ICF with Cough Monitors (CMs), lay individuals who use local strategies to detect smear positive TB cases, has been in effect at Moi Teaching and Referral Hospital, Kenya since 2005. The CM program identified 4411 smear positive in the time period October 2007–September 2009. Multiple community-based strategies were employed.

Method: In order to identify strategies used, both review of work notebooks and data collection forms as well as cough monitor retreats and interviews were carried out.

Results: All CMs utilized similar community sensitization strategies: wearing program message T-Shirts, carrying message labeled bags, distribution of both TB informational posters as well as bilingual fliers. All CMs focused on identification of opinion leaders and initiated contact to establish rapport with the community and allow instruction. Local community gatherings were used for TB health talks. CMs then tailored strategies to their own communities. Strategies used included: Use of cured patients as educators, screening of upper class in primary schools, identification of local gathering locations such as local sports events (to focus on youth), local alcohol brewing dens, bodaboda (bicycle) associations, churches, local schools and women's support groups. CMs distributed donated de-worming medications for children as an entry to households to discuss TB in communities where TB stigma was high. Funerals were utilized for TB health talks. Liaison with private practitioners, pharmacies and herbalists resulted in referrals for those who seek continued care for an ailing cough.

Conclusion: Intensified case finding is an effective strategy for improving early case detection; however, the strategies applied to find cases are not uniform but rather must be innovative, fluid and tailored to each local community to be successful.

PS-101336-13 Reaching the unreached through sputum collection centers for TB diagnosis

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Introduction: Sahyog project of LEPRA Society is an EU and LEPRA UK supported project to strengthen the health system to reduce tribal vulnerability to TB and HIV/AIDS. The project is being implemented in 3 tribal districts of Orissa, India. Sputum testing is pivotal in the success of RNTCP. Accessibility of microscopy center to patients in hilly terrains is poor. Therefore the project is facilitating sputum collection centers (SCCs) for easy collection of sputum in difficult areas.

Objective: To assess the contribution of SCC to RNTCP in 2009 in 16 blocks of 3 districts of Orissa, India.

Methodology: The project has established 180 sputum collection centers. Out of these sputum have been collected from 173 SCCs in 2009 which were analysed in this paper.

Major findings: 1946 new cases (M-1399, F-547) and 1164 (M-836, F-238) follow up cases have been reported to 173 SCCs. The age groups highly benefited are those above 40 from whom 1303 samples were collected and got tested. Out of new sputum samples, 373 (M-279, F-94) were positive. In total 408 TB cases facilitated from SCCs that include 356 Cat-I, 26 Cat-II and 26 Cat-III who were put on

DOTS. The positive case rate from the new sputum samples is 19.17%. By end of 2009, out of 1164 persons follow up sample testing 1055 (90.6%) found negative, contributing significantly to cure rate. Of the 1609 positive cases reported in the entire district, 1334 (82.9%) were from 10 blocks where the project supports and 205 (15.4%) of the cases reported through SCCs. Motivation from SSC holders on regular treatment further lead to the increase in conversion rate (85.7%), cure rate (81.2%) and low defaulter rate (8.64%) especially in an area of physical and socioeconomic hurdles. The functioning of SSCs is equally encouraging in other two adjacent districts. The contribution in case detection is about 40% in spite of extremist threat in the area though other indicators are less satisfactory.

| Particulars | Year | | |
	2008	2009	Total
No of SCC	180	180	180
No of chest symptomatic reported to SCC	1140	1946	3086
Sputum-positive cases diagnosed	210	373	583
Sputum follow-up	252	1164	1416

EPIDEMIOLOGY: TB IN HIGH-BURDEN COUNTRIES/ PUBLIC HEALTH/ SPECIAL POPULATIONS

PS-101041-13 Tuberculosis mortality in New Mexico, USA: a low incidence state

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Purpose: To identify missed opportunities in tuberculosis (TB) prevention, diagnosis, and treatment, and to identify TB mortality risk factors among New Mexico's tuberculosis population.

Design: We used a retrospective cohort study design to identify the cause of death and any missed opportunities in diagnosis and prevention for patients who died with TB in New Mexico from 2007–2009.

Results: Out of 159 patients diagnosed with TB during the study period, 25 (15.7%) patients who died with confirmed TB were included in the final study group. The average age of the patients was 71.7 years (range 36–92); 14 (56%) of 25 patients were female. Ten (40%) of the patients were Hispanic and another 10 (40%) were Native American. Twelve (48%) of the patients were foreign born, with 10 (40%) having been born in Mexico. Only 10 (40%) of the patients were diagnosed by sputum culture, and only 3 (12%) had a cavitary infiltrate on chest radiograph compared to 6 (24%) who had miliary infiltrates on chest radiograph. Of the 25 patients with confirmed TB, 11 (44%) of the cases were pulmonary disease only, with the remaining 56% of cases being extrapulmonary disease only or both pulmonary and extrapulmonary disease. Eight (32%) of the patients had pulmonary disease (either COPD or pulmonary fibrosis), 7 (28%) of the patients had diabetes mellitus, 3 (12%) of the patients were HIV-seropositive, and 9 (36%) of the patients had hypothyroidism. Seventeen (68%) of the deaths were determined to be due to TB-associated disease. The most common missed opportunity for diagnosis and prevention of TB was either a provider delay in diagnosis (60% of cases) or a patient delay in diagnosis (48% of cases).

Conclusion: In this study we confirmed a high tuberculosis-related mortality in a low-incidence state. We identified missed opportunities in diagnosis and prevention that can be used to help reduce future deaths in New Mexico due to tuberculosis.
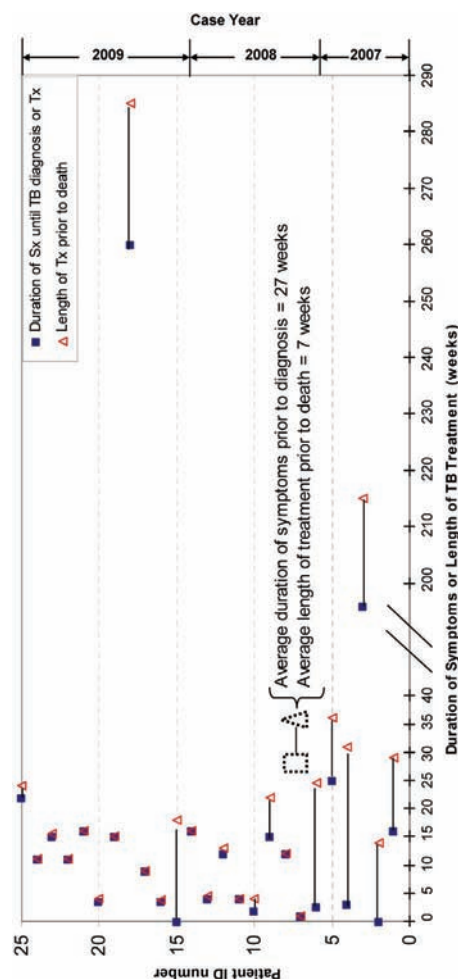
Figure (1) Duration of TB symptoms (weeks) prior to diagnosis or treatment and (2) length of TB treatment (weeks) prior to death. Patients with 0 weeks of symptoms were clinically asymptomatic at the time of diagnosis or had symptoms for fewer than 24 hours. Patients with 0 weeks of treatment were either dead at the time of diagnosis or died before starting TB therapy.

PS-100052-13   First nationwide survey on the resistance to first-line anti-tuberculosis drugs in Ghana

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Setting: Nationwide survey on the resistance to first line anti-tuberculosis drugs conducted in Ghana from 2006–2008.

Objectives: To characterize mycobacterial species causing pulmonary tuberculosis (PTB) in Ghana; determine the levels and pattern of resistance to first line anti-TB drugs among newly diagnosed and previously treated smear-positive PTB patients; determine the prevalence of multidrug-resistant (MDR) TB.

Methods: Two sputum samples from eligible consented smear positive PTB patients were collected for bacteriological analysis. Drug susceptibility testing was performed using the simplified proportion method. Positive cultures were tested against isoniazid, rifampicin, ethambutol and streptomycin.

Results: Among 410 samples, 345 positive cultures (324 new cases and 21 previously treated cases) were obtained with 236 (68.4%) identified as *M. tuberculosis*, 95 (28%) *M. africanum* I, 8 (2.3%) *M. africanum* II (*M. tuberculosis* 'Uganda genotype') and 6 (1.7%) *M. bovis*. The overall drug resistant patterns were: 43 (12.5%) strains resistant to isoniazid (H); 6 (1.7%) to rifampicin (R); 71 (2.6%) to ethambutol (E); 11 (20.6%) to streptomycin (S). MDR (strains that are resistant to at least rifampicin and isoniazid) was observed in 5 (1.4%). For primary drug resistance the results were: H 34 (10.5%), R 2 (0.6%), E 9 (2.8%), S 59 (18.2%) and MDR 1 (0.3%). Acquired drug resistance were: H (42.9%), R 4 (19.0%), E 2 (9.5%), S 10 (4.8%) and MDR 4 (19.0%).

Conclusion: The survey indicates high levels of resistance to first-line anti-TB drugs in Ghana. To monitor the trend, the survey needs to be repeated at regular intervals.

PS-100203-13   Investigation of healthcare seeking patterns of TB patients of urban communities in Shandong Province

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Background: In China, majority of TB patients was from rural areas and government's attention towards urban community is relatively low. This study is to understand the situation of TB service in urban communities, and characteristics and healthcare seeking behaviors of TB patients.

Methods: A survey, with facilitation of structured questionnaires, was conducted to 246 TB patients who were registered during April to September 2008 from urban communities of four middle scale cities of Shandong province. Data regarding gender, age, occupation, household income, medical visit pathway, patients delay, diagnosis delay, and etc. were collected and analyzed.

Results: Comparing with that of rural TB patients, patients from urban communities had various occupation and better incomes, and most of them were under different health insurance schemes. However, patients tended to 'shop around' for medical care after falling ill, and only 12.2% of TB patients chose TB dispensary as their first place for medical consultations. 51.2% of TB patients were diagnosed as TB from service other than TB dispensary. 67% of the patients were delayed for more than 2 weeks from first health visit to diagnosis of TB.

Conclusion: Urban residents had more options to seek care than their rural counterparts. Enhanced health education in urban community is needed, so as to let more people be aware of TB symptoms, and come to right place when fall ill for prompt and proper diagnosis. Diagnosis delay was common, and training of TB to clinicians from primary health facilities should be strengthened, so as to reduce diagnosis delay and transmission risks.

PS-100212-13   Analysis on situation of over-diagnosis and related factors of smear-negative pulmonary TB

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Objective: To explore over-diagnosis and its related factors, provide evidence for increasing diagnosis level of smear-negative tuberculosis.

Method: Four provinces were selected with cluster sampling method which represent high, middle and low of registration rate respectively, according to registration rate of smear negative pulmonary tuberculosis in 2006. One prefecture was selected in each province, and 2 counties in each prefecture, 8 counties (district) in all. Documents and chests films on sixty patients were selected consecutively which selected from the first TB patients diagnosed and registered in every county in 2006. 480 chest films were

read by local county and city smear-negative diagnosis group respectively, and then which re-read by six national experts and two national expert groups respectively. All the data were analyzed with univariate and multivariate logistic regression methods to explore related factors.

Results: Over-diagnosis rate is 26.9%, Risk factors for over-diagnosis included quality of chest film 'C' and quality of chest film 'D', female, over 60 age, PPD history, BCG history, diagnosis of clinical doctors, meanwhile protective factors included diagnosis of smear-negative diagnosis group, referral and central recommendation, no matter analysis on diagnosis result of county, pre-fecture and nation experts on smear-negative tuberculosis.

Conclusion: Diagnosis of smear-negative tuberculosis mainly depends on result of chest film in county dispensaries so far; and few depend on comprehensive diagnosis, such as sputum culture, technology of molecular biological detection, serum antibody detecting and PPD and so on, meanwhile chest quality and diagnosis ability not good which become main cause of over-diagnosis. The study further confirms main related factors which result in increasing and decreasing over-diagnosis, provide evidence for developing national policy and strategy.

PS-100218-13   Lives saved by global TB control efforts

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Background: TB causes an estimated 1.8 million deaths each year, ranking second only to HIV among infectious diseases. Almost all of these deaths could be averted through timely diagnosis and treatment. Efforts to improve TB control were intensified with the launch of the DOTS strategy in the mid-1990s, boosted since 2003 with new financing from the Global Fund (GF), and expanded according to the World Health Organization's Stop TB Strategy since 2006.

Objectives: To estimate the number of lives saved through improved TB control 1995–2008, and to assess whether the 2015 global target for reductions in TB deaths can be achieved.

Methods: Mortality in 1995–2008 was measured from vital registration (VR) data reported to WHO by 89 countries, and estimated indirectly from WHO estimates of TB disease incidence and case fatality rates for countries without VR data. Lives saved were estimated relative to a counterfactual that was defined as standards of care maintained at their 1995 level throughout the 14-year period. Financial data were taken from WHO's global TB database.

Results: Over 1995–2008, 36 million cases were

successfully treated in DOTS programmes. Improved TB control since 1995 averted 3.9 million (range, 1.6–6.2 million) TB deaths excluding PLHIV, and 5.4 million (range, 2.8–9.4 million) TB deaths including PLHIV. Compared with a baseline of 2003, an additional US$3.2 billion (US$0.6 billion from the GF) was available for TB control 2004–2008 in 22 high-burden countries, and 0.8 million TB deaths (range, 0–2 million) including PLHIV were averted. At current rates of decline, the global target to halve the TB mortality rate by 2015 compared with its level in 1990 could be reached.

Conclusions: TB control efforts based on DOTS and the Stop TB Strategy have saved millions of lives since 1995. If current financing is sustained or increased, the 2015 global target for reductions in TB mortality is achievable.

PS-100344-13   Accuracy and completeness of recording of bacteriologically confirmed tuberculosis

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Introduction: TB treatment registers and laboratory records are essential recording and reporting tools in TB control programmes. The accuracy and completeness of routinely collected data are seldom monitored.

Aim: This study used record linkage to assess the accuracy and completeness of TB treatment register data in two South African urban communities.

Methods: All cases of bacteriologically confirmed TB defined as 2 smear positive results and/or at least one culture positive result were included. Record linkage was performed between three data sources: (1) TB treatment registers (2) All smear and culture results from (a) the nearest central laboratory, and (b) the referral hospital laboratory.

Results: The TB treatment registers had 435 TB cases recorded of which 204 (47%) were bacteriologically confirmed cases. An additional 39 cases that were recorded as non-bacteriological cases in the TB treatment register, were reclassified as bacteriologically confirmed. In addition, there were 63 bacteriologically confirmed cases identified from the laboratory databases which were not recorded in the TB treatment register. The final number of bacteriologically confirmed TB cases was 306, an increase of 50%.

Conclusions: The accuracy and completeness of the TB treatment register and central laboratory data were inadequate. A high percentage of bacteriologically confirmed cases from both laboratories were not recorded in the TB treatment registers. We recommend that systems be developed to improve the management of laboratory results and we are currently developing an electronic result management system.

PS-100345-13 Feasibility of capture re-capture methods to assess completeness of recording of TB cases

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Introduction: Reliable surveillance is essential for TB control programs but under-notification of TB cases has been well documented internationally.
Aim: To determine the feasibility of capture-recapture methods to estimate the completeness of TB treatment registration in two high incidence communities.
Methods: Record linking was performed on TB treatment register data and TB sputum results from two central laboratories. Bacteriologically confirmed cases were defined as cases with two positive smears and/or at least one positive culture. To estimate the completeness of TB treatment recording two source and three-source log-linear capture-recapture models were used.
Results: There were 243 bacteriologically confirmed TB cases in the TB treatment register, with an additional 63 cases identified in two central laboratory databases, resulting in 306 bacteriologically confirmed TB cases. Completeness of the TB treatment register was 79%. An initial two-source capture-recapture analysis using the combined laboratory databases estimated 314 (95%CI 307 320) bacteriologically confirmed TB cases, a completeness of recording of 78%. The log-linear model estimated 326 (95%CI 314–355) bacteriologically confirmed TB cases, a completeness of recording of 75%. The log linear model corrected for some positive dependence between data sources in the two-source analysis.
Conclusion: In our study capture-recapture analysis was feasible for estimating completeness of TB registration. Due to considerable register interdependence bias, as our internal validity analysis demonstrates, log-linear capture recapture analysis is preferred. Capture-recapture can be useful for evaluation of the completeness of TB treatment registration, also in resource-limited settings, but methodology and results should be carefully assessed.

PS-100419-13 More TB notifications from women than men in poorer districts: a multivariable analysis in Pakistan

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Background: In most developing countries, more smear-positive tuberculosis (TB) cases are notified from men than women. Reasons for the gender difference are poorly understood. This study investigates whether district level socioeconomic characteristics influence gender differences in smear-positive notifications across Pakistan.
Methods: District level data on socioeconomic variables was compiled from the Pakistan Social and Living Standards Measurement survey and the Pakistan Census. Data on smear-positive notifications from males and females in 2007 was obtained from the National TB Control Programme. A multivariable model adjusting for demographic differences between districts was constructed using log female:male smear-positive notifications as the outcome variable.
Results: Complete data was available for 98 out of 110 districts studied. Indicators of district level under-development such as higher proportion of houses made of mud, lower urbanisation, lower female literacy and higher fertility were significantly associated with more notifications from women than men. Districts with a higher average case load per TB centre and districts with higher self-reported sickness in women than men also had significantly more notifications from women relative to men.
Conclusions: While the relationship between poverty and higher TB rates has been shown in other studies, in this analysis district level under-development was associated with more smear-positive notifications from women than men in Pakistan. The differential effect of poverty on TB in women needs further investigation.

PS-100482-13 Tuberculosis and multiple causes of death in Rio de Janeiro, Brazil: underestimation of TB burden

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Background: Rio de Janeiro city (RJC) has a high burden of tuberculosis (TB), with around 6500 new cases and 400 deaths reported per year. Among HIV-positive individuals, TB is responsible for 9% of deaths when looking at the underlying cause of death. We

studied the magnitude of TB- and TB-HIV-related deaths using multiple causes reported at death and looked for the cases in the TB surveillance system.

Methods: From the Mortality Information System (SIM) of RJC, we extracted all cases with ICD-10 codes ranging from A15 to A19 on any field of the death certificate (DC) from 2001 to 2009. We performed linkage analysis (Reclink software) with the TB reporting system (SINAN) to assess the degree of and factors associated with underreporting in SINAN. Data were analyzed in Stata 9.

Results: We found 5020 cases with TB listed in the DC, after excluding traumatic deaths. The mean annual increase in the number of TB deaths, not including HIV-related, was 36%, 423 to 623 in 2001 and 329 to 522 in 2009. For TB-HIV, the annual increase ranged from 48% to 67%. Compared to TB-HIV cases, TB cases were more likely to be older ($P = 0.01$), male ($P < 0.001$), less educated ($P = 0.001$), white ($P = 0.002$) and be diagnosed with pulmonary TB ($P < 0.001$). Only 38% of all TB deaths reported by DC were reported in SINAN, with 50% of TB-HIV cases reported compared to 35% of TB cases without HIV ($P < 0.001$). Being HIV-positive increased the odds of being reported in SINAN by 1.8-fold (OR = 1.83, 95%CI 1.60–2.10), regardless of TB or TB-HIV reported as underlying or associate cause of death.

Conclusions: TB deaths based on death certificates are substantially underreported in the TB surveillance system, indicating an underestimate of true TB burden in RJC, particularly among TB-HIV co-infected. The estimated TB-HIV death rate was almost double of that reported in the surveillance system. Also striking is the magnitude of underreporting of TB (62%), which may impair the efforts to control both epidemics.

PS-100588-13   Trends of TB notification in Nigeria for 10 years (1999–2009): lessons learnt and way forward

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Background: Nigeria is a federation with 37 states and 774 LGAs. It ranked 4th among the 22 high TB burden countries globally. The estimated incidence for all forms of TB cases in 2009 was 311/100 000 population. The burden of TB in the country is compounded by high HIV prevalence of 4.6%. The DOTS strategy was adopted in 1993 and the recently improved Stop TB strategy in 2006.

Design: A retrospective study of the records of case notification from all LGAs and States providing DOTS services from 1999 to 2009.

Results: The number of all forms of TB cases notified

increased from 23 364 in 1999 to 96 514 in 2009, while that of new smear positive cases also increased from 15 903 in 1999 to 46 026 in 2009. A further analysis of all forms of TB detected from 1999 to 2009 shows that the proportion of smear positive cases has consistently decreased from 68% in 1999 to 48% in 2009 while that of smear negative has increased from 24% in 1999 to 40% in 2009. The proportion of extra-pulmonary TB detected remained consistently low (below 4%). The proportion of Relapses, Failures, RAD and others has remained fairly constant below 4%.

Table National trend of TB cases notified by type and proportion from 2000–2009

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009
New Sm+	68%	67%	64%	63%	61%	57%	52%	54%	51%	51%	48%
Sm−	24%	26%	30%	26%	29%	34%	34%	35%	37%	38%	40%
EPTB	4%	4%	4%	3%	3%	3%	4%	4%	5%	3%	4%
Relapse	4%	3%	3%	3%	3%	2%	3%	3%	3%	3%	3%
Failure				1%	2%	1%	2%	1%	1%	1%	1%
RAD				3%	3%	2%	3%	2%	2%	2%	2%
Others				1%	0%	1%	2%	1%	2%	2%	3%

Conclusions: The gradual decline in the proportion of smear positive TB cases and continuous increase in the proportion of smear negative TB cases notified among all TB cases in 10 years with very low proportion of EPTB is an indication for programme to strengthen the diagnosis of smear-negative TB and EPTB. Specialists in all field of medicine should be comprehensively involved in TB control efforts to increase diagnosis of EPTB and prevent missed opportunities. Developing countries especially those with high HIV prevalence should be supported to strengthen diagnosis of smear-negative TB and EPTB through access to better, simple and affordable diagnostic tools.

PS-100625-13   Nationwide tuberculosis prevalence survey in Bangladesh, 2007-2009

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Aim: Bangladesh ranked 6th among 22 TB high burden countries. The study aims to determine the nationwide prevalence of smear-positive TB in Bangladesh.

Methods: The study was conducted between October 2007 to March 2009. A multi-stage cluster survey of a random sample of 52 098 persons ≥ 15 years were included in 40 clusters (20 urban and 20 rural). Two sputum samples were collected from study participant and tested initially by fluorescence microscopy and confirmed by Ziehl-Neelsen method. The crude, adjusted prevalence rates and 95%CIs were calculated using standard methods.

Results: A total of 33 new smear positive TB cases were detected. The overall crude prevalence of new smear-positive TB was estimated 63.3 per 100 000 (95%CI 43.6–88.9) and adjusted prevalence was 79.4 per 100 000 (95%CI 47.1–133.8). TB cases were more from males (24) and from rural areas (20). The prevalence was highest among persons aged ⩾65 years (150/100 000) and lowest in 15–24 years (43.0/100 000). The prevalence was higher among the lowest SES quintile of population (137.9/100 000).

Conclusions: The overall prevalence of smear-positive TB was significantly lower than previous nationwide survey in Bangladesh in 1987–88. Intensified TB control activities should be continued and increased emphasis should be given to older people, rural populations and lower socioeconomic groups.

PS-100871-13   Effect of public versus private health care access on tuberculosis treatment delay in South Africa

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Background: Prompt tuberculosis (TB) diagnosis and treatment initiation are essential to improve treatment outcomes and TB control. We aimed to determine the duration of patient delay [interval between the onset of symptoms and first health care provider (HCP) visit], health system (HS) delay (interval between first HCP visit and TB treatment started) and total TB treatment delay (patient delay + HS delay) and to investigate the determinates of delay.

Methods: A cross-sectional study of consecutive routinely diagnosed adult TB patients, treated by the National TB control Programme (NTP) conducted at an urban primary health care facility in Khayelitsha, South Africa.

Results: 210 patients (median age 31 yrs; IQR26–39) were enrolled from May–Nov 2009; 46% male and 58% HIV positive. The median duration for total delay, patient delay and HS delay were 31 (IQR18–53), 8 (IQR6–20) and 17 (IQR7–37) days, respectively. More HCP visits before initiation of treatment ($P < 0.001$; $P < 0.001$) and HIV positive status ($P = 0.02$; $P < 0.02$) were independent risk factors for total delay and HS delay respectively. Longer travel time to the clinic ($P = 0.047$) and smear positivity ($P = 0.025$) were associated with patient delay. 27% patients reported first going to a private (non-NTP) HCP (77% to general physicians). With first visit to a private HCP, the number of visits (4; IQR 3–5) and HS delay (25 days; IQR 13–55) were more than with a NTP HCP (3 visits; IQR 2–4; $P < 0.000$) (14 days IQR 7–31; $P = 0.005$). Prescription of antibiotics was the most common first action (89%) of private HCPs, compared to sputum examination at public HCPs (66%).

Conclusions and recommendations: HS delay was longer than patient delay. An initial visit to a private HCP, with subsequent more visits, was the main determinant for HS delay. Engagement and education of private HCPs by the NTP is strongly recommended in this setting.

PS-100891-13   Risk factors for unsuccessful tuberculosis treatment outcomes in Kazakhstan, 2003–2008

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Background: In 1998, the Kazakhstan National Tuberculosis Program implemented the WHO recommended Directly Observed Therapy-Short Course strategy, supporting national targets of 70% new smear positive case detection and 85% treatment success among those detected. Despite meeting targets for case detection, treatment success rates have remained below target. To focus interventions toward national goals, we characterize those patients at highest risk for unsuccessful treatment outcomes.

Methods: All new, adult, smear-positive, pulmonary tuberculosis (PTB) cases registered in the national electronic registry during 2003–2008 were included in this analysis. Logistic regression was employed to determine associations between unsuccessful treatment outcomes (treatment failure, default, or death) and selected clinical, demographic and epidemiologic factors.

Results: Of the 37 659 new, adult, smear-positive PTB patients treated with a standardized first-line drug regimen, 25% had an unsuccessful treatment outcome. Of those, 59% failed treatment, 19% defaulted and 21% died during treatment. Alcoholism was associated with an increased risk of all unsuccessful treatment outcomes, drug use and homelessness with default and death, and unemployment with failure and default. HIV was associated with an increased risk of death. Young adults were at higher risk of failure and default while the risk of death increased with increasing age. Increasing levels of drug resistance were associated with increasing risk of failure.

Conclusions: Socially vulnerable groups were more likely to have unsuccessful treatment outcomes. Patients identified with these risk factors should be targeted for additional support, including second-line drugs for those with MDR-TB.

PS-101266-13 PMDT in Namibia: describing the epidemiology of the 2009 cohort and interim outcomes

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Background: In 2009, Namibia reported 13 332 cases (634/100 000). Drug resistant (DR) TB has been treated since 1999 but was not systematically notified and reported until 2008. The true extent of DR TB therefore remained unknown until the results of the first drug resistance survey (DRS) became available and the national DR TB review meetings were held.
Intervention: A DRTB recording and reporting system was introduced in mid 2008. Quarterly DRTB review meetings to train health workers on case management, using the new data collecting tools and for data verification were initiated in 2009.
Results: 396 DRTB cases were recorded in 2009 (1:0.96 male to female ratio); 275 MDR-TB, 17 extensively drug resistant (XDR) TB; 80 polyresistant TB and 24 commenced on empiric 2nd line regimens without a drug susceptibility testing (DST). Of the MDR-TB patients, 92% had a known HIV status and 57% were HIV positive. The median age was 35; range; 1.5–80, 99.3% had pulmonary MDR-TB while 0.7% had confirmed extrapulmonary MDR-TB. Registration groups in MDR were; failure on category 1 treatment 32%; relapses 29%; category 2 failures 14%; presenting after defaulting 11%; new MDR 9%; transfer ins 3% and 2% classified as 'other'. A 6-month interim analysis of the 63 patients with MDR-TB initiated on treatment in the 1st quarter 2009 showed that 36 (57%) had culture-converted; 10 (16%) were still positive; 12 (19%) had defaulted treatment while 5 (8%) had died.

Table Interim assessment at 6-months for patient treated between January and March 2009

	Culture Positive on Rx	Culture Negative on Rx	Died	Failed	Defaulted/interrupted treatment	Transfer out	Total number evaluated
MDR TB	10	36	5	0	12	0	63
XDR TB	4	0	3	0	0	0	7
Polyresistant TB	4	8	0	0	7	1	20
Suspected MDR/other on empiric treatment	0	2	0	0	1	0	3
TOTAL	18	45	9	0	20	1	93

Conclusion: The high number of MDR-TB cases diagnosed after failing initial treatment (32%) warrants strengthening the monitoring of patients on initial treatment, particularly the 2-month smear and follow up DST for non-converters. The high defaulter rates (19%) at 6 months of MDR-TB treatment suggests the need to focus on comprehensive initial assessments, counselling and patient support.

INNOVATION IN DETECTION OF TB AND DRUG-RESISTANT TB

PS-100315-13 MTBDRplus assay for early diagnosis of multidrug-resistant tuberculosis in southern Viet Nam

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Background: Early diagnosis of multidrug resistant tuberculosis (MDR-TB) plays an important role in interruption of TB transmission and improving treatment outcome. The conventional drug susceptibility testing requires 2 to 4 months for results available. Recently, The GenoType® MTBDRplus test, a commercial line-probe assay, has been evaluated as a rapid test (within 2 days) for detection of major mutations on the *rpo*B gene, *kat*G gene and *inh*A promoter which are associated with rifampicin and isoniazid resistances in *M. tuberculosis* complex isolates. We have found this test high sensitive (>90%) and specific (100%) for detection of rifampicin and Isoniazide resistances in TB isolates. In this study, we assessed the sensitivity and specificity of the test on smear positive sputum samples collected at the microbiology laboratory of Pham Ngoc Thach Hospital, a tertiary TB hospital in the Southern Viet Nam.
Method: 200 smear positive sputum samples were collected and processed for conventional DST and MTBDRplus. All samples with discordant results between the two methods were repeated with MTBDRplus and conventional DST. The reported results were based on the final results of MTBDRplus and conventional DST.
Results: The MTBDRplus detected 86.7% of MDR-TB strains ($n = 65/75$), 93.5% of rifampicin-resistant strains ($n = 72/77$) and 88.7% of isoniazid-resistant strains ($n = 94/106$) against conventional DST. The specificity of MTBDRplus for detection of MDR, Rifampicin resistance and isoniazide-resistance were 96.7%, 96.7% and 97.8%, respectively. The positive predictive value and negative predictive value of this test for MDR-TB detection were 94.2% and 92.2%, respectively.
Conclusion: The MTBDRplus is a rapid and straightforward test, which can be applied on routine smear positive sputum samples for early detection of MDR-TB. The high specificity of this test merits its use in the Programmatic Management of Drug resistant TB in Viet Nam.

PS-100373-13 How useful is line-probe assay for drug susceptibility testing in developing countries?

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Objective: To evaluate the usefulness, feasibility and practical problems of line probe assay to detect drug resistances of clinical *M. tuberculosis* isolates.

Background: The MDR-TB is a major obstacle of its control. It will be necessary to have any rapid method to detect MDR-TB cases. The conventional DST is a time-consuming method. Therefore, molecular based rapid DST method will be considered as a possible solution.

Method: 97 culture strains and 29 smear positive sputum samples were subjected to line probe assay. The strains used were collected during the drug resistance survey in Mongolia in 2007. The sputum samples used were collected from tuberculosis patients who had failure of II Cat treatment. Those strains and sputum samples were tested for conventional drug susceptibility testing on solid medium by proportion method. For the line probe assay system we used Genotype MTBDR plus (Hain lifescience, Germany).

Results: The MTBDR plus test on isolated strains and sputum samples showed high agreement with the conventional DST results (Table).

Table Comparison results

	From culture strains		From sputum samples	
	RMP (*n* = 97)	INH (*n* = 96)	RMP (n = 29)	INH (n = 29)
Sensitivity	0.978	0.917	1.000	0.950
Specificity	1.000	0.915	0.700	0.889
Positive predictive value	1.000	0.903	0.841	0.931
Negative predictive value	0.981	0.927	1.000	0.918
Efficiency	0.990	0.916	0.897	0.931
kappa coefficient	0.979	0.832	0.754	0.839

Conclusions: MTBDR plus kit was evaluated for its sensitivity and specificity using *M. tuberculosis* strains and sputum samples isolated in Mongolia. It showed satisfactory efficiency to the tested samples and indicated its usefulness for the rapid diagnosis of MDR-TB cases. The hybridisation step used TwinCubator® was much better compared to used shaking water bath since it's not time-consuming and better interprets results of the kit. The MTBDR plus kit is useful for detecting MDR-TB cases but is limited to select proper MDR-TB patients' treatment regime. Most developing countries have a shortage of second line TB drugs. Therefore, if planning to introduce rapid test detecting MDR-TB in TB control programme in developing countries, at same time we should increase the second line TB drug supply. Without treatment of diagnosis it will be same as nothing being done.

PS-100256-13 Nucleic acid tests have limited sensitivity for diagnosis of smear-negative TB in Uganda

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Background: Nucleic acid tests are sensitive for identifying *Mycobacterium tuberculosis* when sputum smears for acid-fast bacilli are positive, but less sensitive when they are negative. Few studies have evaluated how nucleic acid tests perform in patients with HIV in high TB-burden countries, where paucibacillary disease appears more common.

Methods: We prospectively enrolled 211 consecutive adults with cough $\geqslant$2 weeks and two negative sputum smears at Mulago Hospital in Kampala, Uganda. We tested a single sputum specimen for *Mycobacterium tuberculosis* DNA using two nucleic acid tests: a novel in-house polymerase chain reaction targeting the secA1 gene, and the commercial GenProbe MTD test. We calculated sensitivity and specificity of the index tests in reference to a gold standard of any positive mycobacterial culture of sputum or bronchoalveolar lavage fluid on solid media. We performed a secondary analysis comparing the index tests to a clinical reference standard including both culture-positive patients, and culture-negative patients who had responded to TB treatment after two months.

Results: Of 211 patients enrolled, one-hundred seventy (81%) were HIV-infected, with median CD4+ T-cell count 78 cells/μL (interquartile range 29–203). Seventy-five patients (36%) had culture-confirmed TB. Sensitivity of MTD was 39% (95%CI 28–51) and that of secA1 was 24% (95%CI 15–35). The tests had equal specificity: 93% (95%CI 86–97) for secA1 and 93% (95%CI 87–97) for MTD. Specificity increased when measured in comparison to the clinical and microbiologic reference standard.

Conclusions: The secA1 and MTD nucleic acid tests had modest sensitivity but high specificity for diagnosing TB in a predominantly HIV-infected population with negative sputum smears. Newer nucleic acid assays targeting multi-copy genes or using nested amplification techniques may more effectively detect *M. tuberculosis* in sputum in pauci-bacillary populations.

PS-100553-13　Detection of *Mycobacterium tuberculosis* rifampicin resistance by polymerase chain reaction

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The goal of this research was detection of the rifampicin-resistance level of *Mycobacterium tuberculosis* infection in the Odesa region of Southwest Ukraine, investigation of the level of mutation at codons 516, 526, 531 in the *rpo*B gene that is contributing into rifampicin-resistance for *M. tuberculosis,* with polymerase chain reaction (PCR), and spread of these mutations in different groups of patients with tuberculosis. Primary and secondary (acquired) resistance to rifampicin of *M. tuberculosis* was 61% and 81% correspondently. Around 45% of DNA-isolates of *M. tuberculosis* had mutation in *kat*G gene. Out of all the mutated strains, 4.8% had a mutation at codon 516 in the *rpo*B gene; 14.3% had a mutation at codon 526, and in 80.9% a mutation at codon 531. Out of all isolates that carried any mutation at codons 516/526/531 in the *rpo*B gene, 93.8% were rifampicin-resistant according to the culture method. Of rifampicin-resistant strains, only 49.5% carried any mutation at codons 516/526/531 in the *rpo*B gene. So, the specificity of this method for rifampicin-resistance detection was 93.8%, and the sensitivity 49.5%. The patients who carried *M. tuberculosis* with the *rpo*B mutation had chronic TB 2.6 times more frequently than those with wild-type strains ($P < 0.05$). At discharge, the smears of patients with wild-type isolates were 1.9 times more frequently negative at microscopy than those of patients with a mutation in the *rpo*B gene of *M. tuberculosis* ($P < 0.05$). The patients who carried *M. tuberculosis* with a mutation in the *rpo*B gene were transferred for outpatient treatment 1.8 times less often than the patients who carried wild-type strains, and 1.9 times more frequently had aborted antituberculosis treatment than did the patients who carried wild-type strains. Our findings support high specifity of the proposed PCR method for rapid detection of *M. tuberculosis* that is resistant to drugs such as rifampicin and for prediction of the outcome of TB-treatment.

PS-100664-13　PCR direct in smear-negative, culture-positive samples in tuberculosis

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Introduction: The value of PCR is well accepted as a method for species characterization in smear positive samples. However, its diagnostic value in the diagnosis of tuberculosis in smear negative samples is still disputed.

Methods: We analysed all PCR direct results of smear negative but culture-positive (*M. tuberculosis*) samples that were collected by our institute of microbiology in the period 1/2008 to 10/2009.

Results: A total number of 62 samples were analysed. 38/62 samples (61%) were tested positive and 24/62 samples (39%) were tested negative on PCR direct. From all sputum samples ($n = 17$) and gastric juice samples ($n = 3$) the PCR direct was positive in 80%, from all materials obtained through bronchoscopic methods however only 55% were tested positive. In 52% of all extra pulmonary samples ($n = 23$; pleura, soft tissue, cerebrospinal fluid, lymph nodes, joints and bones) the result of PCR direct was positive.

Conclusions: PCR direct cannot be considered a reliable method for rapid diagnosis of TB cases with low bacterial load, because it is less sensitive compared to culture. However, its use as complementary method in the examination of sputum samples can be discussed.

PS-100666-13　The implementation of the GenoType MTBDRplus assay (HAIN Lifescience) in the Republic of Georgia

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Background: The emergence of multidrug-resistant (MDR) and extensively resistant (XDR)-TB in the country of Georgia contributes to an enormous public health problem. To enhance detection of drug resistant TB, the implementation of rapid molecular tests for drug resistance are needed. We sought to evaluate the performance of the commercially available Genotype MTBDRplus assay, when integrated into routine lab work, for the detection of resistance to rifampin (RMP) and isoniazid (INH).

Intervention: From June–December 2009, consecutive AFB smear (+) sputum specimens were obtained from TB suspects referred to the National TB Program. Conventional cultures and drug susceptibility testing (DST) using both an absolute concentration method on Löwenstein-Jensen media and broth-based method using the MGIT 960 system were compared to the Genotype MTBDRplus assay. All testing was carried out at the National TB Reference Laboratory in Tbilisi, Georgia.

Results: Among 146 AFB smear (+) sputum specimens, 139 had a positive culture for *M. tuberculosis*. As compared to specimens with a positive culture, the MTBDRplus assay detected any INH resistance in 35/41 (85.4%) isolates, and MDR-TB in 18/19

(94.7%) isolates (Table). There was high agreement between the MTBDRplus assay and conventional DST in MDR-TB detection ($\square$ = 0.91, P < 0.01). The most common resistance mutation for INH was S315T (84%) in the *kat*G codon and S531L (60%) in the *rpo*B codon for RMP. The average turnaround time in days for MTB identification and INH and RMP susceptibility results was shorter with the MTB-DRplus assay (4.1) as compared to using either solid (64.1) or liquid (20.3) cultures.

Table   Performance of the MTBDRplus assay compared to conventional drug susceptibility testing in detecting INH and RMP resistance (n = 139)

	Any INH resistance	INH and RIF resistance (MDR)
Sensitivity	85.4%	94.7%
Specificity	98.0%	98.3%
Positive predictive value	94.6%	90.0%
Negative predictive value	94.1%	99.1%

Conclusions: The MTBDRplus assay had a high sensitivity and specificity in detecting drug resistance in an area with high MDR-TB prevalence. The molecular assay significantly reduced the time to detection of MDR-TB compared to conventional culture and DST and has the potential to greatly impact patient outcomes.

PS-100731-13   Real time PCR for *Mycobacterium tuberculosis* in paucibacillary forms of tuberculosis

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Objective: The early confirmation of diagnosis in paucibacillary forms of tuberculosis, directly in clinical specimens, by Real Time PCR (rt PCR).
Methods: Conventional method's results (Ziehl-Neelsen smear microscopy, Löwenstein-Jensen and MB/BACT cultures, biochemical and cytological parameters) were correlated with detection and quantification of *Mycobacterium tuberculosis* specific sequences, by Real Time PCR technique, directly from the clinical specimens. The MasterPure™ Complete DNA and RNA Purification Kit (Epicentre, Madison, Wisconsin) and Total Nucleic Acids Purification Protocol were used. The Primer Design™ Kit (Primer Design 2X Precision™ MasterMix) is designed for the in vitro quantification of TB genomes. The RT PCR method used LightScanner 32 Instrument/LS32 (Idaho Technology, Salt Lake City, UT).
Results: Prospective study of 15 patients suspected of pulmonary or pleural tuberculosis. There were 15 specimens: 7 from bronchial aspirates (4 positive, 3 negative) and 8 pleural fluids samples (1 positive and

7 negative), rt PCR values where between 11 to 597 copies/microliter. 4/15 patients where rtPCR positive and *M. tuberculosis* culture positive, 9/15 where PCR negative and *M. tuberculosis* culture negative (8 patients confirmed with other diagnostics than TB), 1 was PCR positive, *M. tuberculosis* culture negative. The specificity for *M. tuberculosis* was 93.33% and the sensitivity 90.91%.
Conclusion: Gene amplification techniques are highly sensitive and if the system is adequately standardized, evaluated and precautions for avoiding the contamination are taken, these assays can play a very useful role in early confirmation of diagnosis in paucibacillary forms of tuberculosis.

PS-100899-13   Evaluation of real-time PCR on pleural fluid for the diagnosis of pleural tuberculosis

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Background: Pleural biopsy remains the main method for pleural tuberculosis (PTB) diagnosis, since pleural tissue culture and histopathologic examination are the most accurate for TB. However, a less invasive and risky test would be desirable if it could provide similar or better accuracy. We evaluated the performance of real-time PCR on pleural fluid for PTB diagnosis.
Methods: From January 2003 to July 2005, consecutive PTB suspects undergoing pleural effusion investigation were submitted to thoracocentesis with pleural biopsy. AFB smear, culture for mycobacteria and real-time PCR assay were performed on pleural fluid specimens. AFB smear, culture for mycobacteria and histopathologic examination were performed on pleural tissue specimens. A case of PTB was defined when a positive result was found on AFB smear, culture or histopathologic examination of pleural specimens, or if clinical and radiographic abnormalities were resolved after anti-TB treatment.
Results: A total of 129 patients were included in the study, of which 100 (78%) were diagnosed with PTB. The sensitivity of real-time PCR for PTB diagnosis was 47% (95%CI 37%–57%). Specificity, negative and positive predictive values were 100%, 36% and 100%, respectively.
Conclusion: Although real-time PCR on pleural fluid is a more rapid and less invasive testing, its sensitivity for PTB diagnosis is suboptimal. The high specificity and positive predictive value might be useful to confirm PTB cases.

PS-101144-13   Evaluation of a rapid MGIT™ TBc Identification test for culture confirmation of *M. tuberculosis*

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Background: A culture confirmation test, MGIT™ TBc Identification (TBc ID) (Becton Dickinson, Sparks, MD, USA), for *Mycobacterium tuberculosis* complex has been developed using lateral flow immunochromatographic assay to detect MPB64. We evaluated the performance of the TBc ID test for *M. tuberculosis* complex in liquid culture.
Methods: We applied the TBc ID test to analyze 211 primary positive liquid cultures (within 3 days). No processing or instrumentation was required for this test. Results were compared with those obtained with nucleic acid-based identification. The sensitivity of the TBc ID test was determined using serial dilution of *M. tuberculosis,* and the specificity using 24 non-tuberculous mycobacteria (NTM), mixture of *M. tuberculosis* and NTM, *M. bovis*, *M. africanum*, and Nocardia strains. Results of AFB smear and turbidity of the liquid culture were collected along with each specimen.
Results: The detection limit of the TBc ID test is 3×10^6 CFU/ml, and IS*6110* real-time PCR 5 CFU/ml. Of the 211 samples, 170 (80.6%) contained *M. tuberculosis*. All NTM and Nocardia were found to be negative with no cross-reaction. All *M. tuberculosis* and *M. africanum* cultures were found to be positive, while the results of *M. bovis* and *M. bovis* BCG cultures were negative. Both sensitivity and specificity of the TBc ID test were 100% for *M. tuberculosis*. The turn-around-time for the real-time PCR is four hours (including buffer and sample preparation) and the TBc ID one hour.
Conclusion: With high sensitivity and specificity, the TBc ID test could provide an alternative to currently available identification methods.

PS-100393-13   Acquired rifampicin resistance despite directly observed therapy

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Background: We present a case of acquired rifampicin resistant TB in a 53 year old Vietnamese woman. She presented with haemoptysis in May 2009. A CT showed a left upper lobe cavitatory lesion. Sputum showed acid fast bacilli (AFB) and *Mycobacterium tuberculosis* was cultured using Mycobacteria Growth Indicator Tube 960. Critical-concentration based drug susceptibility testing established isoniazid (0.1 µg/L and 0.4 µg/ml) and streptomycin (1 µg/ml) resistance

and sensitivity to rifampicin and ethambutol. Pyrazinamide was sensitive using the Wayne assay. She was commenced on 6 months of isoniazid, ethambutol, rifampicin and pyrazinamide followed by 3 months of ethambutol and rifampicin. All treatment was carried out under directly observed therapy. Chest X-rays from June 2009 to June 2010 showed stable findings. Culture at 2 months was negative for *M. tuberculosis* on all 3 samples. End of treatment sputum was positive for AFB and culture grew *M. tuberculosis*. Rifampicin *rpo*B gene testing on this sample confirmed acquired rifampicin resistance.
Discussion: This case demonstrates evolved rifampicin resistance with acquisition of *rpo*B gene mutation despite good adherence to therapy and with initial critical-concentration assay showing sensitivity to drugs used. With current DST methods, rather than determining an exact mean inhibitory concentration, a single drug concentration is used to categorize an isolate as either sensitive or resistant. However different genetic mutations that underlie resistance may have different levels of resistance. This may be complicated further by heterogeneity in phenotype resistance. This means that low-level, but clinically significant, rifampicin resistance, is easily missed by automated broth-based methods.
Conclusion: Further studies are needed to determine the correlation of phenotypic resistance levels and treatment outcome however adjustments to the current DST, may enable a more reliable and quantitative measure of susceptibility.

PS-100730-13   Rapid detection, identification and drug susceptibility testing of *M. tuberculosis* strains

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Tuberculosis is a worldwide problem affecting both developing countries and developed countries. The increasing number of HIV+ and AIDS disease also contributes to the increasing number of TB infected. Even though the pandemic of AIDS is not actual threat to the Czech Republic (CZ), due to on-going globalisation and migration connected with it, it is possible that the presently low incidence of TB (around 10) will rise in the future in CZ. We have tested strains from patients coming from around 2 million people (one fifth of population) present in CZ from Jan. 2003 to Dec. 2009. All tested strains were tested according to their susceptibility to 5 AT basic drugs. Total number of 1514 strains of *M. tuberculosis* was isolated. Of all isolated strains 157 strains were resistant for varying combination of AT and out of them 91 strains were MDR-TB (resistant to INH + RMP). In every year TB resistant and MDR-TB strains were analysed from patients according to their domicile

country (we have compared the ratio of domestic and foreigner patients), gender and mean age. In the years 2003 to 2007 the number of resistant strains varied from 13 to 22, but in 2008 their number rose to 49, which was caused by high immigration of workers from Mongolia (traditionally most of the immigrants come from former Soviet Union and Asian countries). In 2009 we have analysed only 20 resistant strains, because the global economic crisis caused the decline of number of immigrants. The same situation was in MDR-TB strains: from 2003 to 2007 their number ranged from 5 to 11, in 2008 it amounted to 38 and in 2009 to 13. All strains were isolated by conventional methods (L-J) and BACTEC MGIT 960 and these methods were used also for drug susceptibility tests. Species of *M. tuberculosis* complex were identified by GenoType® MTBC. It is necessary to find alternative AT for treatment of MDR-TB which is expensive. Other significant problem is insufficient capacity of hospitals for isolated MDR-TB patients.

TB EDUCATION/TRAINING/ COMMUNICATION

PS-101075-13   Better targeting: comparison of the Han and Miao groups of China on education level and media preference

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Objective: This study is intended to examine the difference of education level and media preference of Han and Miao group in China on education level and media preference of TB knowledge so that we can better target difference groups in later TB education and communication.
Methods: The data for this analysis is from two rapid appraisals respectively conducted in 2008 and early 2010, including both quantitative and qualitative study of objects. The analysis focuses on education level and media preference of the two groups. i.e. Han and Miao. In the 2008 study of Han group in Anhui province, a total of 158 respondents (one from each household) including 84 men and 74 women attended the questionnaire survey, 85.4% (135) of which are 25–65 years old. By contrast, in the 2010 study of Miao group in Guizhou province, A total of 105 respondents (one from each household) including 64 men and 40 women attended the questionnaire survey, the average age of which is 49 years old (19–76 years).
Results: In 2008 study, 45% of the Han group respondents are of primary education and below. The general awareness rate of 6-question survey of these respondents is 66.5%, 20% higher than that (48.9%) of the national KAP survey in 2006. By contrast, in 2010 study, 75% of the Miao group respondents are of primary education and below, much higher than that of Han group. An interesting result of this comparison study is in Han group most of them received TB education by face-to-face communication and in Miao group most of them prefer face-to-face communication to learn TB knowledge although the person gives the interpersonal communication is slightly different.
Discussion: This comparison study clearly indicates the variance of education level of Han and Miao group. In the later TB education and communication activities, a levelwise education though interpersonal communication is recommended, which is more productive.

PS-100097-13   Training helps to prevent and control tuberculosis

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In Brazil, tuberculosis is making steady progress on vulnerable populations due to social inequality, and lack of organization of public health. The Global Fund for Tuberculosis FGTB Brazil, aiming to expand and strengthen the DOTS strategy has invested heavily in training for health professionals and civil society. Between May 2007 and July 2009, the FGTB in conjunction with Programs Tuberculosis Control PCT conducted numerous trainings in 57 municipalities supported by FGTB. 5630 health professionals were trained for the implementation of DOTS. To evaluate the trainings a questionnaire was sent to managers of the 57 PCT and the training participants evaluation was also an instrument to evaluate. Replies allowed to reflect on the strategies implemented training and upgrading the upcoming activities. From 57 questionnaires sent, we obtained responses from 32 (56%) districts in total of 897 (44%) trained. PCT managers of 20 municipalities (74%) stated that the training contributed to implementation of DOTS. The update of the content was cited as a positive factor on the courses. The evaluation found that participants learned the content was consistent with their practical needs. It cited as positive the methodology used, getting them aware and empower them to a new position with his own work. It was suggested greater involvement of managers in the courses in order to ensure sustainability of control actions TB. Were cited as important factors and complementary to the success of DOTS: social benefits, qualified human resources and aware, coverage of primary care. Training must be contextualized within a strategy to be implemented. The evaluations of managers and participants showed that FGTB should enhance the understanding of training as a political tool and as an

educational resource for planning and monitoring the actions of TB.

PS-100127-13   Knowledge regarding tuberculosis among TB course participants in Karachi

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Background: It has been reported that most of our General Physicians are treating tuberculosis but their knowledge about diagnosis and treatment of tuberculosis is inadequate and they are not aware of WHO guideline on tuberculosis.
Objective: To assess the current pattern of knowledge regarding tuberculosis, among participants of a certificate course in tuberculosis.
Method: A standardized questionnaire was administered among the participants of 2nd certificate course in tuberculosis at Ojha Institute of Chest Diseases, Karachi. It was filled before start of the course. The questions covered were knowledge related to diagnosis, treatment, National Tuberculosis Program (NTP) guideline, Directly Observed Treatment Short course (DOTS) etc.
Results: Of 128 participants 75 (58.5%) filled the form. 67 (89.3%) responded that TB spread via droplets, 72 (96%) knew the major symptoms of pulmonary tuberculosis, 64 (85.3%) responded that sputum smear is single best investigation for diagnosis, 47 (62.7%) were able to write correct prescription for the intensive phase and 32 (42.7%) for the continuation phase, 15 (20%) knew components of DOTS and 42 (56%) prescribed Fixed Dose Combination (FDCs).
Conclusion: The knowledge of our physicians about tuberculosis diagnosis and treatment is reasonably good but need to improve knowledge about Directly Observed Treatment Short course (DOTS) and National Tuberculosis Program (NTP) guideline.

PS-100225-13   ACSM through innovative method in urban slum setting

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Aim: To measure the impact of an innovative ACSM activity, i.e., street play, by eunuchs on detection rate of tuberculosis in a targeted Delhi slum where literacy rate is low.
Method:
1 The study was conducted over a period of 6 months (April 2009 to September 2009) at Shastri park DMC (Population 1 Lac) under SPMH Chest Clinic.
2 A group of 7 eunuchs were identified from local community. The eunuchs team was trained by professional trainers for street play. The ideas and experiences of eunuchs including movies songs were also incorporated in the training to enhance interest of local community in the street play.
3 Two DMCs namely Shastri Park DMC and Goutam Puri DMC were randomly selected for case control study. A six months intervention was done in Shastri Park DMC. The street plays in the Shastri Park DMC area were performed fortnightly for 6 months (April 2009 to Sep 2009).
4 Two cohort (IInd Qtr 2009 & IIIrd Qtr 2009) case detection rate of both DMCs were analyzed along with same cohorts of previous year.
Result: The case detection rate of the Shastri Park DMC was significantly raised during study period in compression to control DMC (Goutam Puri DMC) and also in compression to same cohorts of previous year.
Conclusion: Street play by eunuchs is an effective mean of ACSM in urban slums.

PS-100332-13   HIV prevention among TB patients in the Chui oblast of Kyrgyzstan by means of patient school

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Background and challenges to implementation: In the last 3 years the number of officially registered cases of HIV-TB co-infection in Kyrgyzstan has grown more than 2.4 times, and mortality among HIV-TB patients has increased. It is crucial to provide interventions on HIV prevention among the most affected groups of TB patients. One of the efficient methods for HIV prevention among TB patients is arranging lessons in the form of 'Patient School' at TB institutions.
Intervention or response: From the year 2006 the KR Ministry of Health (MoH) under technical support of AFEW has been introducing a system for

training patients in terms of TB and HIV the 'Patient School' model. A group of national experts in cooperation with AFEW provided trainings for nurses, developed 'Patient School' module on the basis of recommendations by WHO, and elaborated monitoring tools. The 'Patient School' is conducted during intense stage of residential treatment and offers thematic lessons on TB, HIV, viral hepatitis, STIs.

Results and lessons learnt: 32 nurses of TB agencies in Chui oblast have been trained. Patient School has been organized at 5 TB institutions, including one prison clinic. Results of 2009 monitoring by the MoH show, that the most successful Patient Schools are those at medical institutions, where managing staff provided support for such lessons, allocated special premises, and arranged effective training for medical nurses. According to Chui oblast TB center, adherence to treatment among patients, who have been trained at the 'Patient School', has significantly increased, and 73% of them have completed the treatment successfully.

Conclusions and key recommendations: The training promotes successful TB treatment, increases professional level of medical staff and patients' awareness in terms of TB and HIV, leads to successful outcomes and provides prevention of HIV and STI spread at TB services.

PS-100428-13   Identifying settings for TB prevention education in HIV patients in the Oryol Region, Russia

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Background: Over the last 5 years, the incidence of tuberculosis (TB) among HIV patients in Russia has increased 5.2 times. This study aimed to identify the need for TB prevention education among HIV patients.

Materials and methods: Two groups of HIV-TB patients were observed in one Russian region (Oryol) from 2004 to 2008. Group 1 consisted of 46 cases that were observed in a TB dispensary; Group 2 consisted of 23 cases that were observed in prison settings.

Results: The gender distribution was: 80.4% male and 19.6% female in Group 1; 78.3% male and 21.7% female in Group 2. In Group 1, HIV infection was registered before TB in 81.8% of cases. In Group 2, all patients had HIV before being diagnosed with TB. HIV transmission routes were identified in Group 1 as: drug use 67.4%, sexual intercourse 17.4%, and the transmission route was not identified in the remaining cases. In Group 2, all known transmissions (82.6%) were accounted for drug use. *M. tuberculosis* was identified in 76.0% of patients in Group 1,

among which 20% were resistant to Isoniazide and Rifampicine (MDR-TB); while in Group 2, these figures were 47.8% and 27.3% respectively.

Table   Age distribution by group

Age, years	21–30	31–40	41–50
Group 1, per cent	41.3	50.0	8.7
Group 2, per cent	47.8	39.1	8.7

Conclusions: Assuming that the majority of HIV patients, who later develop TB and who can be reached with TB education, are or have been in prison settings, these settings may be the most suitable for TB prevention education. It is important to develop and implement an integrated TB Prevention Programme for HIV Patients in the Federal Correctional Service of the Russian Federation. The high proportion of drug use among the coinfected patients also calls for intensified case-finding among IDUs.

PS-101110-13   Effective communication programmes control tuberculosis

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Introduction: Sahyog is a project to strengthen the health system in order to reduce tribal vulnerability to TB and HIV/AIDS and is being implemented in 3 districts of Odisha, India. To increase the level of awareness on TB and HIV and stigma reduction through tribal specific communication strategy the project organised different kinds of area specific IEC programmes in 3 districts.

Objective: The objective of the study is to assess the impact on awareness about tuberculosis.

Methodology: A questionnaire administered at the spot to randomly selected participants in the events of 345 Puppet shows, 175 street plays, 261 Film Show, 75 School Education programme, 59 Market Exhibitions, 3 festivals and celebration of 4 special days and analysed. About 68 million population covered.

Major findings: A total of 514 male and 204 female responded to pre IEC questionnaire and the corresponding post IEC respondents include 609 males and 109 females. The familiarity about TB increase from 57.8% to 100% as a result of IEC. Percentage of persons with knowledge on TB increased from 54% to 85%. 32% of respondents knew germ as the cause of TB before IEC and the percentage increased to 45% post IEC session. After IEC sessions increased number of respondants knew about more than one symptoms of tuberculosis. Only 55% of people know that TB is curable before exposed to IEC and after IEC as high as 89.6% of people knew that TB is curable. About 54% of persons knew that TB treatment is available free of cost while after IEC the number of persons with this awareness went up to 85%. The

knowledge about health points for about TB treatment increased after exposure to TB. 87% of respondents knew about govt. health institutions providing TB treatment in contrast to 41% before attending IEC sessions. The consequences of disease was known to 40% people that increased to 80%.

PS-101397-13 The role of MDR-TB patient peer group to keep patient compliance

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Programmatic management of Drug resistant TB (PMDT) has been implemented since August 2009 on Surabaya Municipality at East Java Province, Indonesia. There are 12 patients having treatment. Some problems be faced by them and cause a lot of patients treatment was interrupted. Two of the patients were defaulter and some of them were giving up for several times and denial the treatment. It might become the cause of PMDT failure. The Consillium of PMDT of Dr. Soetomo General Hospital (The PMDT treatment center) decided to make a peer group for the MDR-TB Patients. The peer group was given opportunity to build the norm and made the activity freely. They are become a family and support one another. Some activities were organized, including religious activities, sharing the experience, and improving the life skill. The results are the compliance of the treatment and DOT is increase. One of two defaulters is back and receives the treatment again. All the patients, including their families, feel more comfortable with the situation.

PS-100163-13 Community empowerment: health education and intervention for migrant TB patients living in urban area

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Background: As far as TB among migrants is seriously concerned in Thailand a huge number of undocumented migrants do not access to treatment and care and health service facilities. This study aims to develop the appropriate interventions to control TB among migrants in promoting their access to care in order to early case detection and treatment for stop spreading TB our Thai residents.
Intervention: The project has been implemented by using PRECEDE–PROCEED Model as a conceptual framework with applying health education program

known as MOBILE–MIGRANT Intervention for improving patients' compliance during the treatment in five hospitals located in 3 urban provinces in 2009. This health education and intervention consisted of five activities: 1) patient health conditions' assessment using migrant-centered approaches; 2) mobile-migrant health education program; 3) employer-employee empowerment; 4) migrant volunteer peer support; 5) home visit program and directly observed treatment in community.
Lessons learnt: 138 health personnel and outreach workers have been involved. 420 migrant TB cases were voluntary introduced into this program. 100 out of 420 undocumented non-Thai cases were accepted and randomly enrolled to intervention and control groups. The initial treatment assessment, compliance behaviors, good appointment and DOT were significantly satisfied above 80%. The sputum conversion rate was 85%. The preliminary treatment success rate was about 78% respectively.
Conclusions: The comprehensive health education interventions for improving patients' compliance among migrant TB cases have been successfully implemented. Community involvement and participation and friendly approaching to migrants should be promoted in order to further improve treatment outcome in this vulnerable population.

PS-101154-13 Social inclusion of TB patients to the TB treatment by establishment of TB patients' clubs

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Aim: To reduce number of defaults among TB and MDR-TB patients through establishment of communities of TB patients in Republic of Khakassia of Russian Federation.
Methods: A TB and MDR-TB patients' club 'White Camomile' in Ust-Abakan town on the basis of Russian Red Cross (RRC) local branch was set up in October of 2008. Khakassian Republican Red Cross branch attract TB specialists and Red Cross staff and volunteers and conduct monthly and/or discussions with the TB patients that receiving the Red Cross social support. During club sessions TB patients are provided with comprehensive information about the disease: channels of infection, symptoms, timing and treatment methods. In the end of the discussion/lecture all participants receive information materials. People with a successful experience of recovery are invited to join these discussions in order to raise TB patents' assurance of recovery. A people attending Red Cross club formed a team of volunteers to pro-

vide regular psychosocial care to TB patients who are prone to treatment defaults.

Results: Estimated number of TB patients-participants of the club is 30 people. TB club functions twice a month. Since the beginning of the project 34 club sessions (meetings) were organized. During the period of functioning the TB and MDR-TB patients' club (from October 2008 to March 2010) number of defaults among TB and MDR-TB patients reduced from 6 (4.5%) patients in 2008 to 1 (1.6%) person in 2010. (see Table)

Month/year	Total number of TB patients in Ust-Abakan	Total number of defaults among TB patients in Ust-Abakan	% of defaults among TB patients in Ust-Abakan
11.2007–11.2008	132	6	4.5
11.2008–11.2009	113	4	3.5
11.2009–03.2010 (5 months)	61	1	1.6

Conclusion: Activity of TB and MDR-TB patients' club 'White Camomile' in Ust-Abakan town in the Russian Red Cross local branch contribute to the reduction of number of defaults and provide better results of TB treatment. It is necessary to replicate the experience of these TB clubs in all territories of Republic of Khakassia.

PS-101227-13   Community involvement to fight tuberculosis: experience in Burkina Faso

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Background: Since 2005, the Support Program to the association and community based (PAMAC) implements in association with the NTP, the community of fight against tuberculosis within the framework of the component 4th round GFTAM. The purpose is to contribute to reduce the morbidity and the mortality of tuberculosis. The strategy of intervention contained two sectors: the first was awareness (sensitization) with information, education and communication activities reference of the suspicious cases towards the CDT (center of diagnostic and treatment), a second of community based care including psychosocial support, house calls and office permanence in 18 urban CDT.

Results: From October, 2005 to October, 2009:
— 350 associations involved
— 3597 actors trained community
— 1 777 572 persons sensitize on TB
— A contribution to the detection of 10% of new cases of TB
— 7 534 patients supported by associations
— 12 162 suspicious cases referred to the DTC

Learnt lessons:
— Civil society is capable of responding to the challenges in fight against tuberculosis.
— The existence of capacity strengthening program of associations (PAMAC) facilitated the starting up of this project.
— Close supervision insures the quality of the interventions.
— Traditional healers play an important role in reference to the suspicious cases of tuberculosis to CDT.
— The implication of the patients allows to reduce the stigma and discrimination about tuberculosis.
— A partnership between public health sectors and civil society is possible and allows a synergy of action.

Perspectives: The intensification of the capacities of the civil society allows him to play completely the role of principal recipient for the round 8. A big challenge for a community world molded by experiences.

PS-101242-13   L'intérêt des visites à domicile (VAD) dans le suivi des patients tuberculeux au Burkina Faso

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Contexte : Le Programme d'Appui au Monde Associatif et Communautaire (PAMAC) en collaboration avec le Programme National Tuberculose (PNT) dans le cadre de la mise en œuvre du volet communautaire de lutte contre la Tuberculose soutient 18 associations qui assurent des VAD dans les importants CDT urbains du pays. Les VAD font parties du paquet d'activités de l'accompagnement communautaire.

Objet : Apporter un soutien aux patients tuberculeux, d'identifier et référer les personnes tousseurs vers les CDT. Les VAD sont faites après consentement du patient.

Résultat : D'octobre 2007 à décembre 2009 :
— 4500 patients tuberculeux enregistrés dont 2869 hommes et 1631femmes ;
— 10459 VAD effectuées (3798 repérages de domicile, 6369 soutien psychosocial, 292 recherches d'absents au traitement) ;
— au moins 60% des VAD concernent le soutien psychosocial aux malades tuberculeux ;
— 480 contacts ont été référés et 107 ont été dépistés positifs soit une proportion de personnes dépistées positives sur les références effectuées de 22,29%.

Leçons apprises : Les VAD permettent de :
— apporter un soutien psychosocial aux patients tuberculeux ;
— assurer une sensibilisation sur la TB à l'entourage du patient, réduit donc la stigmatisation et la discrimination envers les patients ;

—superviser l'administration du traitement et renforcer l'adhésion ;

—faciliter la recherche des absents au traitement ;

—renforcer le dépistage précoce de la TB dans l'entourage des patients ;

—aider les personnes atteintes de tuberculose à prendre des décisions concernant leur situation.

Conclusion : Les VAD ont permis un accompagnement des patients tuberculeux au niveau des CDT et la détection précoce de la tuberculose chez les cas contacts. Cependant, son impact sur le traitement est avant tout qualitatif. La majorité des malades saluent le soutien qu'ils reçoivent à travers cet accompagnement.

PS-100303-13   Promoting quality TB services through single TB brand

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Background: Tuberculosis (TB) is a major public health challenge in Pakistan. Public-Private Partnership (PPM) is an important component of National TB Control Program's (NTP's) vision for TB control. A decentralized and integrated approach has been designed to bring all healthcare providers and health systems levels into the TB control loop, thus enabling equitable distribution of quality TB services for all. Free diagnostic and treatment services are available in 5000 establishments located in 135 districts covering three regions of Pakistan. There are also more than 2000 private TB establishments providing either diagnostic, treatment or both services at the same place.

Challenge: By large the flow and absorption of TB patients is a big challenge, a large number of TB patients end up in seeking health care from the private sector health care establishments as opposed to be absorbed by the primary and secondary health care establishments of public sector. Anecdotal evidence suggests that there has hardly been an effort to promote public health establishments offering quality diagnostic and treatment services in Pakistan.

Intervention: 5800 public and private sector TB diagnostic and treatment centers branded all over the country by using a single brand 'Together Life Wins' through promotional boards, saying 'Free TB Diagnostic and Treatment Services are available'.

Impact: Trust among TB patients on seeking health care from public sector establishments. Improvement in quality of services at private sector establishments.

Conclusion: Promotion of quality TB services lead to improved quality of life of TB patients.

PS-100498-13   Tuberculosis control: radio campaign in five urban areas in Mexico

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Background and challenges to implementation: In November 2006, USAID funded a project to design an Information-Education-Communication (IEC) strategy for Mexico. In 2008 received funding to implement a radio campaign in areas with high TB prevalence rates.

Intervention or response: Materials and methodologies were designed and validated in the pilot test to address needs identified in the pre- and post-campaign surveys.

Objectives and indicators: The radio campaign's overall strategic objective was to improve basic knowledge of TB in the target population, as well as to effect changes in behavior and practices.

Results and lessons learnt: People decided to seek care upon recognizing the symptoms and being advised to do so by a healthcare professional at the health center. Educational talks were mentioned as another important source of information for people to visit a healthcare facility. Respondents mentioned family members, neighbors, information heard on the radio, and other sources as factors that influenced them in deciding to seek care.

Conclusions and key recommendations:
- 20% of those seeking care were motivated because they heard on the radio.
- Significant improvement in knowledge of symptoms, transmission, and treatment.
- Contribution to increase the number of lab tests.
- Strengthening local capacity for designing and implementing a Monitoring and Evaluation plan.
- Generation of tools and data that aid in understanding the populations' KAB.

Recommendations for future IEC activities: Three detailed types of recommendations were considered: designing IEC activities, mass media campaigns, and messages.

PS-100741-13 Impact of World TB Day Commemorations on political commitment, community awareness and involvement

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Background and challenges to implementation: Advocacy, Communication and Social mobilization is among the key components of the Stop TB strategy. Low advocacy and awareness of TB among political leaders and community has been identified as main challenges for Afghanistan. The World TB Day (WTBD) in 2009 was used as an opportunity to sensitize political leaders and mobilize community. We assessed the impact of WTBD 2009 campaigns on political commitment, health workers information, community awareness and involvement in TB program.
Interventions: A number of activities were held before and during the climax including school children march, TV/Radio Spots, round tables, interviews and community gathering and distribution of IEC materials to health facilities and community. WTBD Celebration impact was assessed through interview with health workers, clients, political, and community leaders, Stop TB Partnership (STP) and TB Task force members.
Results and lessons learnt: WTBD commemoration increased the TB awareness among 32/150 (21%) school children, 28/62 (45%) doctors, 22/62 (35.5%) nurses, 126/600 (21%) clients and 10/30 (33.3%) religious leaders. STP increased political commitment as well strengthen coordination among members, such as holding of regular TB Task force and STP meetings, involvement of private sectors and traders in TB control program. WTBD provided opportunity for expansion of STP into southwest and west regions of the country.
Conclusions and key recommendations: The WTBD commemorations provide a good platform to sensitize political leaders and community on TB. More resources should be allocated to WTBD commemoration in order to cover more activities and attain wide coverage.

PS-100763-13 Involvement of media for advocacy and communication in TB control: a preliminary report from South I

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Background: The four southern metropolitan cities of India which has a total population of 14.4 million.
Objectives: To increase media involvement for advocacy and communication in TB control and to create a platform for their participation, To sensitize media professionals to problems in TB control and to enable them to put out correct, verified and timely information. To recognize media initiatives in TB reporting.
Methodology: A descriptive report on involving media professionals in TB control between March 2009 to February 2010 in the four metropolitan cities of South India. About 339 media personalities belonging to print, television and radio and 26 colleges with journalism students were enlisted and invited for a TB sensitization workshop. A website was developed exclusively for media professionals' participation and to track their participation.
Results: About 90 media professionals and 144 media students underwent TB sensitization workshop. Post sensitization results showed increased participation from print, television and radio in terms of publishing of several in-depth articles on TB, telecasting television and radio spots respectively. College owned community radio had also participated in creating awareness on TB. The website registered 76 652 total hits with 210 average hits per day and 24 average visitors per day.
Conclusion: The above analysis has shown that reaching out to media professionals in a sustained manner would yield promising outputs in terms of increase coverage and reporting on TB. Documenting such efforts and outcomes will help in evolving a framework for media participation.

PS-101143-13 Action through partnership for AIDS management

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Aim: To prevent new infection of HIV through family physicians to control AIDS epidemic.
Objective: To increase awareness and capacity building for diagnosis, management of HIV of private/ physicians, with subsequent referral for management.
Background: It is estimated that private sector hospitals and private physicians in India are providing approximately 80% of health services. The training program and CME by the program managers do not target the private physician. Family physicians are first contact points and enjoy the confidence of patient and public and play a model role in the society. In the paper objective, methodology using a 'tiered approach', (approved by MCI and IMA) method of evaluation, problem faced in organizing and conducting the training sessions and allocation of the budgetary provisions has been discussed in detail.
Methodology: The Indian Medical Association (IMA) and the Clinton Foundation HIV/AIDS Initiative (CHAI), in collaboration with National AIDS Control Organization (NACO) as a part of the Physicians Training Initiative (PTI) undertook the ambitious task of training a large number of private doctors (150 000) across multiple locations through facilitator-led training sessions using a 'tiered approach'. In the

first phase 56 913 doctors were trained in one and half year's time in 13 states at multiple locations.

Result: Evaluation of training program revealed substantial increase in the knowledge level (18–22%), awareness regarding the national protocol for HIV testing, about diagnostic facilities/centers that undertake HIV tests resulted increase (12%) in referral of HIV positive patients to ART, centers.

Recommendation: Involving of family physicians in National program.

Table   Number of doctors trained in the program statewide

States	Number of sessions	Planned attendance	Actual attendance	% attendance
A.P.	273	13 600	13 426	98.72
Bihar	15	750	739	98.53
Goa	3	150	144	96.00
Gujrat	122	6 100	5 845	95.82
Haryana	4	200	182	91.00
Himachal Pradesh	10	500	492	98.40
Kerala	146	7 300	7 192	98.52
Madhya Pradesh	71	3 550	3 526	99.32
Maharashtra	39	1 950	1 865	95.64
Orissa	43	2 150	2 038	94.79
Tamilnadu	42	2 100	1 939	92.33
U.P.	174	8 700	8 588	98.71
West Bengal	216	10 800	10 385	96.16
		58 410	56 913	97.44
ToT		560	552	
Total trained			57 465	

PS-101309-13   Communities' awareness, perception and intended treatment-seeking behaviour on pulmonary tuberculosis

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Aim: In Ethiopia, the burden of tuberculosis (TB) remains high, while patient delays and huge backlog of untreated cases risk continued transmission. This study was carried out to assess communities' knowledge, perception and treatment-seeking behaviour for pulmonary TB symptoms.

Methods: Through a two-stage cluster sampling technique, 90 villages in the 10 districts were selected from which 9 households were randomly selected from each village. A total of 826 adult households heads were interviewed by trained interviewers using a structured questionnaire. Data were gathered from both female and male household heads.

Results: Respondents' general awareness of pulmonary tuberculosis was reasonably good. The median knowledge score was 4 (range 0–6). Knowledge scores below the median were significantly more prevalent among rural residents, older age groups and men. Respondents would tend to delay treatment if they ever had persistent cough for at least 4 weeks. Persistent cough for more than 3 weeks and additional symptoms were regarded as signs for seeking treatment from public health facilities by most respondents. Respondents with a higher knowledge score tended to seek treatment early in public health facilities if they had persistent cough.

Conclusions: Rural communities have poor perception of PTB which could potentially contribute to patient delay. Context-specific community-based health education, advocacy and communication interventions need to be introduced as part of the TB control programme to improve public awareness and case detection in Ethiopia.

PS-100363-13   Tuberculosis training of physicians who perform immigration medical examinations

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Background: Approximately 450 000 immigrants and 70 000 refugees arrive in the United States yearly after completing an overseas medical examination, which includes screening for tuberculosis (TB) disease. In 2008, the Division of Global Migration and Quarantine (DGMQ), Centers for Disease Control and Prevention (CDC), began offering comprehensive regional trainings to panel physicians, the doctors designated by United States Consulates to perform the mandated medical examinations.

Methods: The trainings occur over 2½ days and concentrate primarily on TB diagnosis: chest radiography, smear microscopy, culture, drug susceptibility testing (DST), and directly observed therapy (DOT) throughout initiation and continuation phases.

Results: Since 2008, DGMQ has conducted four regional trainings, in Amman, Jordan; Nairobi, Kenya; Manila, Republic of the Philippines; and New Delhi, India. Over 150 panel physicians from 28 countries have attended. In 2010, two more trainings are planned: in Accra, Ghana, and Santo Domingo, Dominican Republic.

Conclusion: Regional panel physician trainings are an important method of increasing the practicing knowledge of physicians screening for TB. Their continuation can help to benefit non U.S.-bound populations as well as U.S.-bound immigrants and refugees and therefore strengthen global TB control efforts.

PS-100790-13   Rapid scale-up of TB-HIV training through training of trainers of HIV-service organizations, Uganda

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Background: In 2007 a 26 district situation analysis in Uganda showed that few health workers had been trained in TB-HIV co-management despite the previous launch of policy guidelines on TB-HIV collaboration and the availability of PEPFAR funds. In 2008 and 2009, the TB Control Assistance Program (TB CAP), funded by USAID, supported TB-HIV training of health workers in 12 districts which resulted in great improvement in the TB-HIV indicators but did not impact national performance. TB CAP staff thus began technical assistance to PEPFAR-supported organizations supporting provision of TB and TB-HIV services.

Intervention: In November 2008 TB CAP staff performed a needs assessment which showed that training in TB-HIV by partners was generally lacking and not standardized. Capacity was built for partners to scale up TB-HIV trainings; two training of trainers (ToT) workshops using the U.S. Centers for Disease Control and Prevention Teachback methodology were conducted by TB CAP and Ministry of Health (MoH) TB and HIV program staff. Pre and post tests were administered for all participants who were supported to develop training action plans to scale up training of health workers in the districts and sites supported by their organizations. Thereafter, TBCAP provided follow-up support to the trainers as they implemented their action plans.

Results: Key knowledge gaps were identified from the pre-test results. Fifty-one staff from 15 partner and partner-supported organizations were trained as trainers. They have trained 437 health workers in TB-HIV co-management. Including MoH staff among the facilitators was important for technical input and guidance on policy issues. Initial reports from some of the partners and partner-supported districts indicate improvement in TB-HIV indicators.

Conclusions: Creating a pool of trainers in each organization enabled rapid scale-up of TB-HIV training of operational level health workers in partner-supported sites and districts.

PS-100774-13   AIDSS.ORG: a web-based interface to promote TB-HIV research in developing countries

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AIDSS.ORG is a powerful free-of-charge web-based interface (www.aidss.org) that assists medical personnel from developing countries to create a platform for data capture and analysis. Scientific research: We have developed AIDSS.ORG specifically to host studies on TB and HIV. AIDSS.ORG allows researchers to enter data from multiple sites using one system and provides tools for real-time data analysis, which helps to early identify risk factors. Using a geo-location aware data system, research can be undertaken to study disease distribution and modes of transmission. AIDSS.ORG is also a platform and search engine for journals that provide free-of-charge full-text access to their articles. AIDSS.ORG aims to empower medical scientist from developing countries to participate in international research. This will create a sustainable and growing network of enthusiastic researchers around the globe that eventually improves national health care systems by implementing evidence-based medicine into a cultural context. AIDSS.ORG is an open-source inspired medical research data and tool-sharing platform committed to training and long-term projects. Mobile access to data entry, management, sharing, analysis and results allows researchers from the remote areas to participate in international research. Surveillance: AIDSS.ORG can be implemented at sites of disease notification. The National Health Systems can use AIDSS.ORG to daily enter laboratory test results into a geo-location aware system with real-time data analysis. This provides early disease notification to the governments and to identify hot spots of disease transmission. Security and Privacy: Of primary importance to AIDSS.ORG is data protection and security. AIDSS.ORG uses internationally certified Thawte SSL 256 Bit data encryption to protect data from unauthorized access. Our user authentication system defines special access rights for certain users to avoid misuse. AIDSS.ORG provides an hourly backup system.

PS-100658-13   Family focus and community orientation in tuberculosis control

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Aim: To assess tuberculosis (TB) control actions in the context of Family Health Teams, concerning the dimensions family focus and community orientation in a harbor municipality in Brazilian Northeastern Region.

Methods: A cross-sectional evaluative research was carried out in 2008, with 84 health workers. The instrument Primary Care Assessment Tool was used, validated and adapted to assess tuberculosis care in Brazil. The respondent answered each question according to a pre-determined scale, (Likert's scale) ranging from zero to five. Data were analyzed according to frequency and median. Each indicator was ordered, and identified the value that was in the central position. The classification 'non-satisfactory' was attributed to the values next to 1 and 2, around 3 and 4 'regular', and around 5 'satisfactory'.

Results: The outcomes shows that 67.9% of the health workers evaluation the contact cases with diagnostic exams; 63,1% used radiological test; 64.3% includes the household to face up to disease; 77.4% have identified risk factors; 41.7% articulate with other sectors to find solutions for the identified problems, 73.8% of them realize search of cases; 40.5% provides inputs for sputum collection; 50% take educational actions in the community; 14.3% recognize social participation in TB control. Among the investigated variables, the 'intersectorial action' and 'inputs for sputum collection' presented a regular performance (average value even 4). Also, 'social participation in TB control strategy' presented non-satisfactory performance (value even 1). The others variables presented satisfactory values.

Conclusion: Therefore, the efficiency of such services requires the taking of actions that give special attention to family and community, and the development of abilities to create new spaces for health workers to act and to strengthen the articulation with other sectors of society.

MDR-TB EPIDEMIOLOGY: AFRICA AND SOUTH AMERICA

PS-100078-13   High mortality in HIV-positive and HIV-negative patients with XDR-TB in Eastern Cape, South Africa

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Background: Tuberculosis is a leading cause of morbidity and mortality worldwide. Patients with extensively drug-resistant tuberculosis (XDR-TB) have had high mortality rates, especially when co-infected with HIV.

Methods: A retrospective cohort study of the first 274 patients diagnosed with XDR-TB in Eastern Cape (EC) Province, South Africa, all patients diagnosed October 2006 January 2008. EC has treated multidrug-resistant (MDR) TB since 2000. Patients were hospitalized for treatment until monthly sputum specimens were culture-negative. Data were censored 365 days after treatment initiation.

Results: Sixty-five (23.7%) patients died prior to starting XDR-TB treatment. Among 206 patients starting treatment, 195 had known HIV status: 108 (55%) were HIV-positive and 87 (45%) were HIV-negative. Within the first year of treatment, 95 patients died (46%), 55/108 HIV-positive patients (51%) and 31/87 HIV-negative patients (36%) ($P = 0.03$). Mortality was similar in HIV-negative patients and HIV-positive patients on ARVs (42%), but higher in HIV-positive patients not on ARVs (58%) ($P = 0.04$). HIV-negative patients had serious adverse events requiring withdrawal of anti-TB drugs more frequently than HIV-positive patients, regardless of ARVs ($P = 0.33$). Risk factors for death included low starting body weight, smear positivity at treatment start, start-
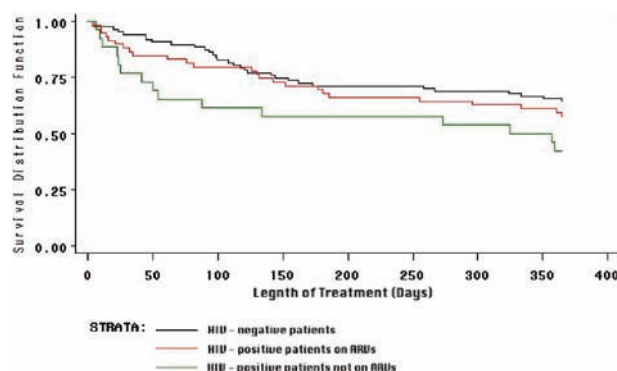
Figure   12-month survival of patients HIV-negative, HIV-positive on ARVs, and HIV-positive not on ARVs.

ing treatment at 25–42 years of age, and duration of previous TB treatment.

Conclusion: Experience in Eastern Cape, South Africa, suggests rapid testing for first- and second-line drug resistance and prompt initiation of treatment for both TB and HIV could improve survival of persons with XDR-TB. According to South Africa's new guidelines, patients with XDR-TB should be initiated on ARVs rapidly after XDR-TB treatment initiation, regardless of CD4+ cell count.

PS-101197-13   Resistance pattern of *M. tuberculosis* in a social security hospital in Peru: 4 years experience

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Background: Social Security hospitals have DST for almost all Tuberculosis (TB) drugs. This study was design in order to know the sensitivity patterns of Mycobacterium Tuberculosis strains in our patients.

Design: A transversal descriptive study was made in a Social Security hospital in Lima-Peru (Edgardo Rebagliati Martins National Hospital) between January 2005 and December 2009. 121 smear positive sputum samples drug susceptibility testing (DST) were made with the Löwenstein-Jensen culture (proportion method). The drug susceptibility was made for 10 drugs. Four scenarios were proposed: DST susceptible to isoniazid (INH) and rifampicin (RMP), DST resistant to INH and susceptible to RMP, DST susceptible to INH and resistant to RMP, and MDR DST.

Results: If the strains are susceptible (S) to INH and RMP, over 94% of them will be susceptible to ethambutol (E) and pyrazinamide (Z), but only 48% will be susceptible to streptomicyn (SM). This strains show over 100% sensitivity to ciprofloxacin (Cpx) and amikacin (Amk), but only 89% to kanamycin (Km). The analysis show that if the strain is resistant (R) to INH, it will be 100% susceptible to Cpx, Amk, Z and thiocetazone (Thz) and 80% to Km. All strains were resistant to Ethionamide (ETH). Resistance to Amk is related to 100% resistance to Km. Strains resistant to first-line drugs are also resistant to Km until 70%. Resistant to Km is related to 35% resistance to Amk In XDR strains, 100% will have Km resistance and 60% resistance to Amk. This is related to first- and second-line drug resistance.

Conclusions: This study has shown that MDR strains pattern should not use SM for its high resistance pattern, and instead use K or amikacin, when resistance to K exists. Ciprofloxacin is a good second line drug for MDR strains (93% sensitivity). In sensitive strains, resistance to E and Z is 5%. A better comprehension of the sensitivity patterns will help to give a better treatment for our patients.

Drug	First scenario		Second scenario		Third scenario		MDR scenario		
	INH	RMP	INH	RMP	INH	RMP	INH	RMP	Total
Pattern	S	S	R	S	S	R	R	R	
DST, *n*	74		5		12		30		121
%	61.16		4.13		9.92		24.79		100.00

Drug susceptibility	N	%	n	%	n	%	n	%
E	71	95.95	4	80.00	10	83.33	13	43.33
Z	70	94.59	5	100.0	10	83.33	12	40.00
E and Z	71	95.95	4	80.00	9	75.00	5	16.67
E or Z	74	100.00	5	100.0	10	83.33	17	56.67
SM	36	48.65	1	20.0	6	50.00	3	10.00
Cpx	73	98.65	5	100.0	12	100.00	28	93.33
Km	66	89.19	4	80.0	10	83.33	18	60.00
Amk	74	100.00	5	100.0	12	100.00	23	76.67
ETH	0	0.00	0	0.0	0	0.00	0	0.00
Thz	50	74.63	5	100.0	9	81.82	8	27.59

PS-101341-13   The impact of HIV coinfection on MDR-TB treatment effectiveness in Brazil

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Background: The effect of HIV coinfection on MDR-TB treatment outcome has not been fully investigated in Brazil.

Objective: To determine the impact of HIV infection on the effectiveness of MDR-TB treatment.

Methods: In a retrospective cohort analysis (Jan 2000–Dec 2007), 2299 patients admitted for MDR-TB standardized treatment were analyzed. Data were collected from the Brazilian Surveillance System up to September 2009 and analyzed by logistic regression model to assess the association of HIV infection adjusted for other risk factors related to MDR-TB treatment outcome.

Results: Characteristics of study population were: mean age 39.2 years, predominantly male (65.2%) and low schooling level (62% <7 years). Half of them had been treated more than 3 times for TB and 96% presented acquired resistance. The prevalence of HIV infection was 7%. This analysis demonstrates that HIV infection reduces the possibility of cure in around 50% (OR = 0.56, CI 95% 0.40–0.78) compared with the uninfected patients. Other factors associated to cure were: age (OR = 1.01% CI 95% 1.01–1.02), male (OR = 0.81% CI 95% 0.66–0.99), drug addiction (OR = 0.44% CI 95% 0.24–0.82), alcoholism (OR = 0.59% CI 95% 0.42–0.82), hospitalization (OR = 0.69% CI 95% 0.57–0.86), mental illness (OR = 0.40% CI 95% 0.17–0.97) and chest X-ray with bilateral involvement (OR = 0.71% CI 95% 0.56–0.90). The HIV status was an independent risk factor associated with cure of MDR-TB when adjusted for age, gender, drug addiction, alcoholism,

previous TB treatment, hospitalization, mental illness and bilateral radiological involvement.

Conclusion: It was demonstrated that HIV infection reduced the effectiveness of MDR-TB treatment in this population. Therefore, the implementation of a multidisciplinary and interprogrammatic care in assisting HIV coinfected patients is crucial, including supervised treatment in Brazilian health facilities.

PS-100091-13   Anti-tuberculosis drug-resistant pattern against first- and second-line drugs

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Setting: Nigeria ranks 4th among the TB High Burden Countries in the world. It has an estimated MDR-TB prevalence of 1.9% and 9.3% among New and retreatment TB patients respectively. There has not been a national drug resistant survey to quantify the MDR-TB burden in the country. The objective of the study is to determine the prevalence of MDR-TB among new and category II failure TB patients in South West Nigeria.

Design: A retrospective study of the records of patients attending TB clinics in Oyo and Osun states in South West Nigeria whose sputum or culture samples were sent to the supranational lab at the Institute of Tropical Medicine, Antwerp, Belgium between 2007 and 2009.

Results: Data for 61 (23 New and 38 Category II) patients were available. There were 36 (59.0%) males and 25 (41.0%) females. Among the 23 patients without history of previous TB treatment the prevalence of resistance to first and second line drugs were Isoniazid (4.3%), Rifampicin (8.7%), Ethambutol (0%), Streptomycin (4.3%), Capreomycin (13%) and Ofloxacin (4.3%). There was no case of MDR-TB among New patients. Among the 34 category II patients, resistance to first and second line drugs were Isoniazid (81.5%), Rifampicin (81.5%) Ethambutol (60.5%), Streptomycin (85.8%), Capreomycin (0%), Ofloxacin (5.3%), Prothionamide (7.9%), Ethionamide (13.2%), Kanamycin (2.6%). MDR-TB was present in 76.3% while 57.9% were resistant to all first line anti TB drugs. Among those diagnosed with MDR-TB, there was no patient diagnosed as XDR-TB.

Conclusions: MDR-TB resistance rates were high among category II TB patients. There is need to carry out a TB resistance survey to quantify the MDR-TB situation. The development of laboratory capacity for culture and DST and the provision of second line drugs to patients already diagnosed needs to be urgently addressed.

PS-100180-13   Spatiotemporal analysis of drug-susceptible and drug-resistant tuberculosis in Lima, Peru

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Background: A better understanding of how drug resistance initially emerges and subsequently spreads may facilitate control of drug-resistant tuberculosis. We aimed to test the hypotheses that the spatial and temporal distribution of multidrug-resistant tuberculosis cases differs from that of other tuberculosis cases and that information about the location and date of diagnosis of tuberculosis patients can improve our ability to predict drug resistance among individuals initiating tuberculosis treatment.

Methods: All eligible incident cases of tuberculosis ($n = 11\,711$) in two districts of Lima, Peru during 2005–7 were included. Clinical and demographic information was collected and home addresses were georeferenced. The spatiotemporal distribution of multidrug-resistant cases and that of other cases were estimated and compared using Ripley's K statistic. Four different multivariate regression models for predicting drug-resistant tuberculosis, one with non-spatial variables only and three with additional spatial or spatiotemporal variables, were constructed and compared on the basis of their predictive performance.

Results: Among 11 711 tuberculosis cases 445 (3.8%) were found to have multidrug resistance. Spatial clustering of patients with confirmed multidrug-resistant disease was similar to that of other patients in 2005 and 2006; near the end of the study period in 2007, cases with confirmed multidrug-resistant disease were found to be more tightly clustered. In multivariate modeling, the addition of spatial or spatiotemporal information improved the performance the predictive model; the area under the ROC curve increased significantly from 0.67 for the non-spatial model to 0.72 ~ 0.75 for the three spatial or spatiotemporal models.

Conclusion: Information on location of tuberculosis patients may be used to improve our understanding of the transmission dynamics of tuberculosis and the prediction of drug resistance among new cases.

PS-100318-13   Resistance to TB drugs in KwaZulu-Natal: causes and prospects for control

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Background: In response to the XDR-TB outbreak reported in 2005 at Church of Scotland Hospital (COSH) in uMzinyathi District, KwaZulu-Natal (KZN), an investigation was carried out to determine if XDR-TB was occurring elsewhere in the province, and to develop hypotheses for the rise in drug resistance with a view to developing a strategy for control of MDR and XDR-TB in the province and elsewhere.
Method: TB incidence and treatment success rates, for each of the 11 districts in KZN, were obtained from the provincial electronic TB register for the years 2002–2007. The results of culture and drug sensitivity tests for the years 2002 to 2007 in each of the districts were compiled and culture taking practices were compared to the number of MDR-TB cases. Interviews were conducted with key personnel in affected sites.
Results: In 2007, 2799, or 2.3% of 119 218 notified TB cases in the province, were MDR, and of these 270 (9.6%) were XDR. The two worst affected districts were uMzinyathi where 226, or 4.1% of 5522 notified TB cases, were MDR, and of these 120 (53%) were XDR; and uMkhanyakude where 337, or 4.8% of 6991 notified TB cases, were MDR, but of these only four (1.2%) were XDR. The worst affected medical centre was COSH where 164 (9.8%) of notified TB cases were MDR and of these 99 (60%) were XDR.
Conclusion: Very high rates of XDR-TB in the province are only found in uMzinyathi district even though MDR-TB is common throughout the province. XDR may have surged in the pre-ART era due to early TB and HIV programme integration in overcrowded and poorly ventilated facilities. To prevent further spread better management of both susceptible and resistant TB is needed including treatment supervision, infection control and HIV management.

PS-100750-13   National survey on the prevalence of anti-tuberculosis drug resistance in the Kingdom of Swaziland

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Setting: Swaziland is among the countries with the highest burden of both tuberculosis (TB) and HIV infection. Several cases of XDR-TB were already reported but there is no recent drug resistance prevalence data in the country. Such information is crucial to assess adequacy of treatment guidelines and to anticipate potential of MDR and XDR-TB nosocomial epidemic among HIV infected patients.
Objectives: To measure the prevalence of MDR-TB among NC and PTC and to describe the prevalence of resistance to first and second line drugs (among MDR-TB patients) in order to revise current treatment guidelines if needed.
Design: A cross-sectional survey was designed based on the WHO/Union guidelines for surveillance of antituberculosis drug resistance using a systematic sampling method. Smear positive adult TB patients were eligible for the study. Patients with severe haemoptysis or taking anti-tuberculosis drugs (except if failures) were excluded. One sputum specimen was systematically collected in any smear positive adult. Specimens were shipped weekly to the Supranational Laboratory for Mycobacteria in Borstel (Germany) where culture and DST were performed.
Results: During the recruitment period, 420 NC and 419 PTC were included in the study. Of these, 412 and 401, respectively, could be cultured. Drug susceptibility patterns are available for a total of 352 NC and 296 PTC. Any drug resistance was 15.6 and 49.4% in NC and PTC, respectively. The prevalence of MDR-TB was 7.7% (95%CI 5.1–11.0) in NC; and 33.4% (95%CI 28.1–39.1)in PTC. HIV co-infection was significantly associated with a higher prevalence of MDR ($P = 0.010$). Among MDR, 45.7% were resistant to ethionamide. Resistance to ofloxacin was 6.4%. There was 1 (0.2%) XDR case.
Conclusions: With more than 6% MDR-TB prevalence among NC, Swaziland belongs to the high MDR prevalence countries. These results, and the high HIV-TB co-infection in the country, claim for revision of current guidelines with rapid identification of MDR-TB and adapted regimens.

PS-100762-13   Drug resistance patterns in a tuberculosis prevalence survey in Western Kenya

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Background: Limited data exist on the prevalence of resistance to anti-TB drugs in populations with high rates of TB and HIV in Kenya. A TB prevalence survey was conducted among 20 566 persons ≥15 years of age in Rarieda and Gem districts, western Kenya. The prevalence of bacteriologically confirmed pulmo-

nary TB (PTB) was 6.0 per 1000. In the province, HIV prevalence is 15%.

Objective: To determine patterns of resistance to first-line anti-TB drugs among *Mycobacterium tuberculosis*) isolates obtained from a TB prevalence survey in western Kenya.

Methods: Cultures were done for survey participants with positive smears for acid-fast bacilli, chest radiograph abnormalities or symptoms suggestive of PTB. Participants with bacteriologically confirmed PTB were offered HIV testing. Strains of *M. tuberculosis* complex from Löwenstein-Jensen slopes were subjected to drug susceptibility testing (DST) to isoniazid (INH), rifampicin (RMP), streptomycin (SM), and ethambutol (EMB) using the conventional resistant ratio method.

Results: Of 123 persons with PTB, 102 (83%) had an isolate available for DST. Mean age was 45 years (standard deviation 19 years), 53 (52%) were female, 8 (8%) reported prior TB treatment, and 43 (49%) of 88 patients with HIV results were HIV-positive. Of 102 isolates, 79 (77%) were sensitive to all drugs. 19/102 (19%) were resistant to INH; of these, 13 were INH mono-resistant and 6 were resistant to INH plus EMB (2), SM (3) or both (1). No multi-drug resistant TB (MDR-TB), defined as resistance to both INH and RMP, was detected. Two of 19 (10%) patients with INH resistance reported prior TB treatment. Gender, age, reported prior TB treatment, and HIV status were not significantly associated with resistance patterns.

Discussion: Low rates of drug resistance and absence of MDR-TB in a population with high rates of TB and HIV is good news for the national TB program. Continued monitoring of drug resistant TB is warranted in this high-risk population.

PS-100953-13 Epidemiology of Isoniazid resistance in Namibia and the implication for INH prophylaxis

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Background: Namibian guidelines recommend Isoniazid Preventive Therapy (IPT) for HIV positive patients in whom active tuberculosis (TB) has been ruled out. The TB drug resistance situation in Namibia was not known till the first drug resistance survey (DRS) was carried out in 2008. The survey shed light on levels of drug resistance in new and retreatment cases by age, sex and geographic region. A detailed analysis of Isoniazid resistance is presented here and the potential implications for IPT discussed.

Method: The study was a prospective study including all 34 districts in Namibia. PTB suspects presenting

to health facilities between 1 May 2008 and 31 January 2009 had a survey form completed and sputum samples collected. Sputum smear positive specimens (SSP)were included in the survey. TB culture and drug sensitivity testing (C/DST) and a HIV test were performed on the sputum sample. Smear negative samples were excluded. Double data entry was performed in Epidata version 3.1 and analysed in Epidata Analysis V.2.2.1.171.

Results: 1702 (26% of SSP cases reported in 2008) were recruited from a proposed 1800 sample. Of these 1451 grew Mycobacterium Tuberculosis (21% of SSP cases reported 2008). 1054 of these were new cases and 354 were previously treated. Cases with any Isoniazid (INH) resistance were 20% (95%CI 17.7–21.8). INH resistance in new patients was 14% (95%CI 11.5–15.5) and in retreatment cases 38% (95%CI 33.5–43.6). HIV prevalence was 47% in all cases. There was no significant association between HIV status and INH resistance.

Conclusions: There is high INH resistance in smear positive PTB patients. TB prophylaxis should therefore be revisited in light of the high INH resistance. This study was however limited to smear positive cases. Given the significantly higher number of smear negative PTB cases among HIV positive patients; there is need to conduct a similar study using more sensitive tests such as culture to assess the significance of these findings.

PS-101067-13 MDR-TB prevalence in category II treatment cases in the littoral region in Cameroon

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Setting: All 31 Basic Management Units (BMU) of Tuberculosis (TB) in Littoral Region of Cameroon.

Objective: To determine the prevalence of multi-drug resistance (MDR) in previously treated TB patients starting a category II treatment and examine its frequency in the different subgroups of retreatment cases.

Design: A prospective descriptive study. During 2009, all previously treated TB patients put on cat. II treatment in the BMUs of the Littoral Region were consecutively enrolled. A sputum sample for each case was collected for culture and drug susceptibility testing. Cultures were done at the regional reference laboratory in Douala and DST was performed at the National Reference Laboratory in Yaoundé.

Results: A total of 434 patients were registered for a cat II treatment in the Littoral Region. Cultures of sputum samples were done for 269 (61.9%) patients. Positive cultures and DST results were obtained from

171 (63.5%) of the 269 patients; the results of 39 cultures are still not available. 21 (12.3%) of the patients harbored MDR strains. MDR strains were found in 52.1% of failures, in 13.4% of relapses, and in 3.8% of defaulters.

Conclusions: Among retreatment patients in the Littoral Region, defaulters are at a high risk of harboring MDR strains. Routine collection of sputum for culture and DST from patients starting a cat. II treatment in a regional setting in Cameroon for monitoring anti-TB drug resistance appears feasible. For rendering the MDR-TB surveillance system more efficient coverage of sputum collection in the target group has to be improved.

PS-101244-13   Anti-tuberculosis drugs resistance in high HIV prevalence settings: Malawi, Kenya and Uganda

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Rising tuberculosis (TB) rates in sub-Saharan Africa are largely attributable to the HIV epidemic. Emergence of multi- and extensive-drug resistance tuberculosis (MDR and XDR) in high HIV prevalence areas is a serious concern but remains poorly documented in many countries. We present results of three antituberculosis drug resistance surveys conducted in high HIV prevalence areas supported by MSF HIV and TB programs: Homa Bay district (Kenya), Chiradzulu district (Malawi) and West Nile region (Uganda). The same cross-sectional survey based on the WHO/IUATLD guidelines for surveillance of antituberculosis drug resistance was designed in the three areas. Consecutive newly diagnosed smear positive adult patients detected in each area were included. Previously treated cases were also enrolled during the intake period for new cases. Culture and drug susceptibility testing for 1st and 2nd line drugs (in case of MDR) were performed at the Institute of Tropical Medicine in Antwerp (Belgium). A total of 1073 patients were included, resulting in 88.4% positive cultures, 5.4% contamination, and 0.7% non-tuberculosis mycobacteria. Drug susceptibility patterns were available for 950 patients (354 in Homa Bay, 300 in Chiradzulu and 296 in West Nile region). Almost 80% were susceptible to all 1st line drugs: 83.3% in Homa Bay, 81.0% in Chiradzulu, and 73.0% in West Nile region. Among resistant strains, any resistance to isoniazid was the most frequently detected: 9.9% in Homa Bay, 11.0% in Chiradzulu, and 15.9% in West Nile region. Fourteen MDR cases were identified. The prevalence of MDR-TB was 1.4% (95%CI 0.5–3.3)

in Homa Bay; 2.0% (95%CI 0.7–4.3) in Chiradzulu; and 0.7% (95%CI 0.1–2.4) in West Nile region. No XDR-TB cases were detected. The prevalence of MDR-TB was low in the three regions. There was a relatively high rate of primary isoniazid resistance, thus increasing the chances of relapse with current standardised short course chemotherapy.

PS-101331-13   Second-line drug resistance among MDR-TB failure cases in the RSA

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Background: South Africa implemented a standardized program for management of MDR-TB in 2000. A prospective cohort of 2079 MDR-TB patients were enrolled till 2004 to determine treatment outcomes, of which the failure rate was 9% and default rates 20.4%. Prior to 2000 use of second-line drugs (SLD) were limited, thus expecting resistance to be low. The high default rates could result in XDR-TB (resistance to fluoroquinolones and injectables). Among this cohort, culture conversion before month 9 was found to be associated with treatment success.
Aim: To determine the impact of second line drug resistance among MDR-TB failure cases on culture conversion.
Methods: Patient, treatment data and sputum specimens were collected at baseline and monthly until failure. At MRC, specimens were cultured on LJ slants and stored at 4°C. Visible colonies were scraped from the slant, DNA was isolated by boiling. SLD resistance was determined with the Genotype® MTBDRsl kit.
Results: SLD resistance were determined for 103/186 failure cases; among which 23.3% (24/103) was XDR, 20.4% (21/103) pre-XDR (resistant to Ofloxacin or Kanamycin), and 55.3% (57/103) only MDR. For 94 of these with culture conversion data, 64.9% (61) failed to convert by month 9, while 35.1% did. 83.3% (20/24) XDR patients, 57.1% (12/21) pre-XDR and 49.1% (28/57) only-MDR patients never converted. Logistic regression analysis indicated XDR-TB patients are more likely not to convert (OR 8.2 $P = 0.008$) than only-MDRs. Comparing to pre-XDR, XDR-TB failures also have a higher risk not to convert (OR 5.83).
Conclusions: Among non-converters, any resistance to SLD was only found in 50.1%, showing failure and late conversion occur also among only-MDRs. Case holding should be enforced for all patients, irrespective of SLD resistance. SLD testing should be done as early as possible.

PS-101386-13   Prevalence of primary MDR-TB in not at risk PTB patients in Lima, Peru

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Introduction: In areas with high MDR-TB prevalence, initial drug susceptibility testing (DST) is recommended for patients with a high risk for MDR. However, this approach might miss a substantial proportion of MDR-TB in the general population. We studied primary MDR in not at risk patients in a northeastern district of Lima.

Methods: Between April 2008 and October 2009 we enrolled 585 new sputum smear-positive TB patients. We excluded 85 patients who reported alcohol or drug use, previous contact with MDR-TB cases, a history of imprisonment and patients who were HIV positive. Sputum was cultured in Löwenstein-Jensen media and DST for first line drugs was determined using the proportion method.

Results: We detected 7.2% (95%CI 5.2, 9.9) patients with MDR-TB. None of the 2.3% that reported previous TB prophylaxis had MDR-TB. We found no significant differences in duration of cough, mean body mass index, median age or gender between MDR and non MDR-TB patients. In patients who reported a non MDR-TB household contact, 4.7% (7/148) had primary MDR-TB versus 8.1% (28/347) of those reporting no household contact ($P = 0.2$). However, 22.2% (4/18) of patients with a contact that died with TB, had MDR-TB versus 6.5% (31/477) of those who had a TB contact that survived ($P = 0.01$).

Conclusions: We detected high rates of primary MDR-TB in a population without known risk factors for drug resistance. This prompts further investigation into setting-specific transmission patterns and revision of current initial DST practices.

PS-101469-13   Factors associated with multidrug-resistant tuberculosis in Kenya, 2009

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Background: Multidrug-resistant tuberculosis (MDR-TB) and weak health systems threaten global tuberculosis control. Kenya is 13th among 22 high TB burden countries and currently has an estimated 2016 MDR-TB patient.

Setting: Forty two hospitals with MDR-TB patients.

Objective: To determine factors associated with MDR-TB.

Methods: This was a case-control study. Cases were MDR-TB patients while controls were sputum smear positive TB patients with clinical and bacteriological response by the fifth month of treatment with first-line drugs. Consenting MDR-TB patients were enrolled and two unmatched controls randomly selected per case from the facility TB register. Data was obtained through interviews and record reviews, entered and analyzed using Epi-info software.

Results: Eighty one cases and 162 controls were enrolled over three months. There were no statistically significant differences with respect to baseline sociodemographic characteristics. Cases were more likely to have history of previous TB treatment (AOR = 85, 95%CI = 29.7–243.3; $P < 0.0001$) and be of foreign origin (AOR = 5.5, 95%CI = 1.4–21.8; $P = 0.007$). Case-patients who had received TB treatment under DOT (AOR = 0.23, 95%CI = 0.1–0.6; $P = 0.002$) and those with a positive HIV status (AOR = 0.34, 95%CI = 0.1–0.9; $P = 0.025$) were less likely to have MDR-TB.

Conclusions: MDR-TB was associated with previous TB treatment, and being of foreign origin. Use of DOT was protective. The protective effect of HIV positive serostatus reflects selective survival of HIV negative MDR-TB patients. We recommend strengthening of MDR-TB surveillance among previously treated TB patients and refugees, and active MDR-TB case finding among HIV infected TB patients. Access to TB care and implementation of DOT should be strengthened.

PS-101509-13   Multidrug-resistant tuberculosis surveillance in Brazil

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Background: In 1993, the Ministry of Health implemented the Reportable Disease Information System (SINAN), a tool for collecting and processing data from reporting health diseases, including tuberculosis (TB). In 2000 we implemented the National Epidemiological Surveillance System of Multidrug Resistant TB (NS/MDR-TB), which acts independently of SINAN although the information generated in the systems is complementary. One of the aims of the NS/MDR-TB is to evaluate the reported cases profile, ensuring the surveillance of the disease and the treatment effectiveness.

Aim: To identify the MDR-TB situation in the SINAN database in Brazil. Intervention: we conducted a linkage between the SINAN database (2001 to 2008) and the NS/MDR-TB database (2006 to 2008), according to Coeli and Camargo, 2002.

Results: SINAN had 731 061 TB cases and NS/MDR-TB 1206 cases. After linkage, 2412 pairs were considered true, it was the same individual. Among the 2412 pairs, 1259 (52%) were the same infection, five years before MDR-TB notification, 63 (3%) different infections and 7 (0.3%) duplicates. Finally, 1085 MDR-TB cases were found in two systems. 51 (4.5%)

NS/MDR-TB registers with history of TB treatment were not found in SINAN. Among the 1238 cases in SINAN with treatment outcome as MDR-TB, 411 (33%) were registered in NS/MDR-TB.

Conclusions: Differences were found in the TB cases reported in the two systems, suggesting MDR-TB cases may be being reported directly to the NS/MDR-TB. Furthermore, the results suggest problems in SINAN treatment outcome data, since only 33% of TB cases were finished as MDR-TB were in NS/MDR-TB. The linkage data is a work that aims to qualify the surveillance data, becoming an important tool when working with more than one data source. The National TB Control Program will conduct the training of the human resources in health services, so that the linkage of data can be incorporated into the routine of the TB Control Programs.

PS-100540-13   Integration of HIV testing in routine TB drug resistance surveillance in Kenya

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Background and purpose: In 2009 Kenya reported a tenfold increase in TB cases since 1990 mostly attributed HIV pandemic. 88% of patients in 2009 were tested for HIV with 44% TB-HIV co infection. HIV status is not routinely included in MDR-TB surveillance. HIV information is now readily available with the scaling up of routine HIV testing in TB patients (coverage >80%) and should be incorporated into routine MDR-TB surveillance. We explored how to implement routine HIV testing under programmatic conditions in this in a country with high HIV and relatively low MDR-TB.

Methods: Reviewed the screening and data collection system. HIV status was integrated in the culture request form from 1st January 2009. Analysis was done of this newly created dataset wherein HIV status and drug susceptibility status was linked.

Results: Analysis of 2009 data showed the key challenge was completeness of data for all parameters. The preliminary data showed no significant relationship between HIV status and MDR-TB status or resistance to first line drugs. MDR-TB prevalence seemed slightly higher than earlier reported. Significantly more women are HIV positive than men and MDR-TB seems more prevalent below 25 years olds.

Conclusion: 2009 data provided new insights in the relationship between HIV-status and MDR-TB and data collection and screening system that will help the program develop interventions to strengthen screening and develop key indicators.

PS-100196-13   Options for dealing with MDR-TB in hard-to-reach districts of Northern Kenya

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Aim: The current MDR-TB situation in northern Kenya is strongly influenced by cross boarder issues in Somalia. This paper describes the situation as it has developed over the last few years and provides options available for controlling or minimizing the crisis which is growing rapidly, and has the potential to explode.

Methods: A desk review and case study approaches, backed by retrospective data, abstracted from the TB registers and records since 2003. Interviews findings from program and clinical personnel used to supplement quantitative data.

Results: Twenty cases reported since 2003 to 2009. Initially 1 to 2 cases per year were idenified through culture and DST. However, in 2008, 5 cases notified and 6 in 2009. Two thirds of these cases were identified within the refugee camps which hold thousands of refugees from Somalia. All cases were HIV negative. This is different epidemic to the southern African epidemic.

Conclusion: There is a growing MDR-TB problem in Northern districts of Kenya most likely because of refugee population that needs to be urgently controlled.

Recommendations: There is need to establish an MDR-TB program in this region. Policy and programmatic options for the Kenyan tuberculosis program need to be developed to prevent cross-border transmission of disease.

ABSTRACT PRESENTATIONS SUNDAY 14 NOVEMBER 2010

FEATURED ABSTRACT PRESENTATIONS

TB-HIV CLINICAL AND EPIDEMIOLOGICAL RESEARCH AND CARE

FA-101232-14   TB-HIV/AIDS surveillance in Cuba, 1986-2009

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In the Americas, because of HIV/AIDS, health situation becomes worse due to tuberculosis (TB) and HIV co infection. We describe the trend and current situation of HIV/AIDS and TB in Cuba. Data on Surveillance of HIV and TB from both the Ministry of Public Health and the 'Pedro Kourí' Institute were analyzed. Since 1986 up to December 2009, around 34 millions of HIV tests (1.6 million/year) have been performed; 12217 HIV seropositive persons (HSP) (5.3×10^5) were identified; 4938 AIDS cases (2.0 per 10^5) and 2127 deaths; 77.5% of HSP were 15–34 years old; 86% were infected by homo-bisexual intercourse; 16.3% by heterosexual, 0.3% by blood-borne transmission, and 0.4% perinatally. Cumulative figures of HSP increased from 3230 in 2000 to 10090 in 2009. TB cases notification decreased from 1133 in 1979 (11.6×10^5 population) to 503 in 1991 (4.7×10^5), with a reversion up to 1574 (14.2×10^5) in 1994; it declined to 5.8×10^5 in 2009. Overall primary TB drug-resistance decreased from 8.3% in 1986–95 to 7.1% in 2005 and primary multidrug resistance was 0.7%, 0.0%, 0.9% and 0.0% in 1996, 1998, 2000 and 2005, respectively. Among HSP, 526 (4.7%) TB cases have been diagnosed; around 45 of them by nosocomial transmission in 1993–94. TB-HIV co infection although its increase seems to keep low figures but need close attention by the TB elimination plan.

FA-100392-14   Sputum conversion rate among multidrug-resistant TB-HIV co-infected patients in Donetsk, Ukraine

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Aim: Ukraine has a high burden of multidrug-resistant (MDR) TB. MDR-TB is prevalent among TB patients co-infected with HIV and effective treatment methods are urgently needed. In 2007 the Donetsk Oblast of Ukraine (4.5 million people) initiated a model MDR-TB project with the support of the 'Development of Ukraine' foundation and WHO which aims to provide such high quality treatment. Aim of this research is to make the preliminary assessment of the treatment of MDR-TB-HIV co-infected patients during intensive treatment phase.
Methods: In the framework of the project, four specialized MDR-TB departments were opened that provide treatment for co-infected patients. One of these departments for 70 patients was opened on the basis of Donetsk Oblast clinical TB Hospital.
Results: 30 (41.1%) out of 73 patients with TB-HIV co-infection who received intensive treatment in this department in 2009 were diagnosed as MDR-TB patients. Sputum conversion after 6 months of treatment was achieved in 14 (46.7%) cases. In 4 (13.3%) cases sputum conversion was achieved in 9–12 months. All patients received standard treatment regimens with 2nd line TB drugs in accordance with MDR-TB Protocol based on WHO recommendations. 7 (23.3%) patients died, in 5 (16.7%) cases treatment default was registered.
Conclusions: Taking into account the high complexity of this patient group, these preliminary results are encouraging. Measures are taken to ensure appropriate follow-up until the end of the treatment with particular emphasis on support during the continuation phase.

FA-100402-14   Clinical, radiologic features, TB treatment outcomes among isoniazid preventive therapy participants

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Background and objective: To evaluate clinical, radiological manifestation and treatment outcomes of IPT exposed, either 6 month or longer, TB patients among persons living with HIV (PLWH) during IPT trial.
Methods: A clinical trial in which individuals seeking IPT and potentially interested in IPT trial were referred to study clinics. All eligible individuals received first six months of INH, and continued with coded

medication (for half was placebo and the other half INH). Participants were followed for five years, individuals suspected to have had TB, with any duration of cough, fever, night sweating, weight loss, hemoptysis and lymphadenopathy >2 cm, were evaluated. Categorization: 'definite TB' if >1 culture or >2 smears were positive for acid-fast bacilli (AFB), 'probable' if one smear was AFB positive or biopsy consistent with TB, or 'possible' based on symptoms and clinical response to anti-tuberculosis treatment.

Results: Out of 1995 (46% of 4331 screened) participants enrolled, 76 (3.8%) TB patients were diagnosed, and 32 (42% of 76) were exposed to IPT for >6 months. 28 (37% of 76) had positive baseline tuberculin skin test. From 76 total there were 44 (58%) definite, 10 (13%) and 22 (29% possible TB cases. Only 11 (14% of 76 total and 25% definite) were AFB smear positive. There were 4 (11% of 38 with available sensitivity report) INH mono-resistant cases. Treatment outcome was known for 74, with 93% treatment success rate. Treatment outcomes did not differ by either CD4 status or length of IPT exposure.

Conclusions: In our cohort of PLWH, early detection and treatment resulted in high treatment success rate. INH mono-resistance TB did not appear to be a problem among IPT exposed TB patients. With high smear negative rate, culture was the mainstay of TB diagnosis in our cohort.

FA-100858-14   Risk factors for early mortality in a cohort of TB-HIV patients commencing antiretroviral therapy

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Background: Early mortality in TB-HIV co-infected patients has been reported in sub-Saharan Africa. However, the incidence and predictors of early mortality are uncertain.

Objectives: To determine the incidence of mortality among TB-HIV patients commencing ART and predictors of mortality.

Methodology: In a prospective cohort study on tuberculosis immune reconstitution inflammatory syndrome (TB-IRIS), we enrolled consecutive adults with confirmed TB-HIV, CD4 cell count <250 cells/μL, and no liver or renal dysfunction. The patients were on TB treatment before initiation of ART and we evaluated them at 2, 4, 8, 12 and 24 weeks. We used Kaplan-Meier survival analysis and Cox proportional hazards modelling to determine the incidence and predictors of mortality.

Table Hazards for mortality in a TB-HIV cohort initiating antiretroviral therapy

Characteristics	Unadjusted hazard ratio (P value)	Full adjusted odds (P value)	Final model
Age (per yr)	1.03 (0.085)	—	—
Sex (Female)	1.81 (0.120)	2.21 (0.050)	—
WHO stage	0.93 (0.864)	1.5 (0.371)	—
Haemoglobin (g/dL) IQR	0.87 (0.099)	—	—
CD4 counts (cells/μL)	1.0 (0.640)	—	—
Started ART	0.03 (<0.001)	0.14 (<0.001)	0.12 (<0.001)
TB IRIS	0.35 (0.054)	0.59 (0.376)	—
Age (5 year increment)	1.18 (0.085)	1.20 (0.079)	1.19 (0.072)
Haemoglobin >10.5 g/dL	Reference	Reference	Reference
9.5 to 10.4 g/dL	2.5 (0.092)	7.90 (0.047)	2.58 (0.087)
8.0 to 9.4 g/dL	1.81 (0.287)	7.16 (0.077)	2.50 (0.105)
<8 g/dL	2.43 (0.116)	4.58 (0.374)	1.41 (0.542)
CD4 counts increase per 50 cells/μL	0.94 (0.0640)	0.77 (0.140)	—

Results: From December 2007 to July 2009, 257 TB-HIV patients were enrolled with median age 34 years (IQR 28–39), and CD4 count 53 cells/μL (IQR 21–134). ART was started a median 43 days (IQR 28.5–43) after TB treatment. The 6-month risk of mortality was 11.8% (95%CI 8.4–16.6%). Initiation of ART was the only factor significantly associated with reduced mortality (HR 0.03 (95%CI 0.12–0.61, $P < 0.001$) after adjusting for age, sex, WHO clinical stage, CD4 count, TB-IRIS and haemoglobin level. Failure to start ART was due to mortality from severe disease (10 patients), loss (5 patients) and patient refusal (1 patient). Most causes of death 21/34 (60%) were due to opportunistic infections.

Conclusion: ART initiation is the principal determinant of survival among patients with co-morbid TB-HIV disease and concerted efforts should be made to ensure early treatment.

FA-101226-14   Lopinavir pharmacokinetics during concomitant rifabutin administration in patients

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Background: HIV-associated mycobacterial diseases are difficult to treat due to drug-drug interactions between rifamycins and antiretroviral drugs. The use of ritonavir-boosted lopinavir (LPV/r) plus adjusted dose rifabutin (aRFB) is recommended in HIV-infected subjects with mycobacterial disease (MD), but the pharmacokinetic properties of LPV/r in association with rifabutin have not yet been described in clinical studies.

Methods: HIV-infected subjects with MD prospectively enrolled in two clinical studies were included in this analysis. All patients received LPV/r (standard dose) + aRFB (150 mg $3\times$/week). 12-hour full pharmacokinetic LPV curves were recorded 2 (T1) and 10 weeks (T2) after starting combined therapy. A control curve for LPV was recorded 10 weeks after stopping aRFB (T3). LPV plasma concentrations were measured with a validated HPLC-UV method. PK parameters were calculated with a standard non-compartmental method (InnaPhase Kinetica, v4).

Results: 23 patients were included. Median LPV PK values at T1, T2, and T3 were, respectively: AUC 0–12h: 145, 158, 108 μg.h/mL; Ctrough: 10, 10, 8 μg/mL; Cmax: 16, 16, 13 μg/mL; and CL/F: 0.042, 0.038, 0.049 L/h/kg. Paired LPV PK parameters at T1, T2 and T3 were compared in 11 patients with complete measurements: no statistical difference was detected between T1 and T2; Ctrough was significantly higher at T1 than at T3 ($P = 0.01$). LPV/r was well tolerated and none of the patients experienced any adverse events of grade >III.

Conclusions: LPV plasma exposure was not decreased by intermittent rifabutin, despite the inductive effect of this drug on CYP3A4 enzymes. In fact, our data show a significant increase in LPV Ctrough, which suggests that other factors may be involved, from the downregulated expression of hepatic LPV transporters caused by rifabutin, to an inhibitory effect on CYP450 enzymes by coadministered anti-TB drugs.

FA-101273-14   Consistency of TB-specific IFN-γ responses in HIV-1 infected women during and after pregnancy

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Background: Interferon-gamma (IFN-γ) release assays (IGRAs) are useful to detect latent tuberculosis infection (LTBI). The influence of the pregnancy and postpartum period on IGRA responses and assay reproducibility is poorly defined.

Methods: In a historical cohort of 18 HIV-1 infected pregnant women with positive T-SPOT.*TB* IGRAs at 32 weeks gestation, IGRAs were conducted on
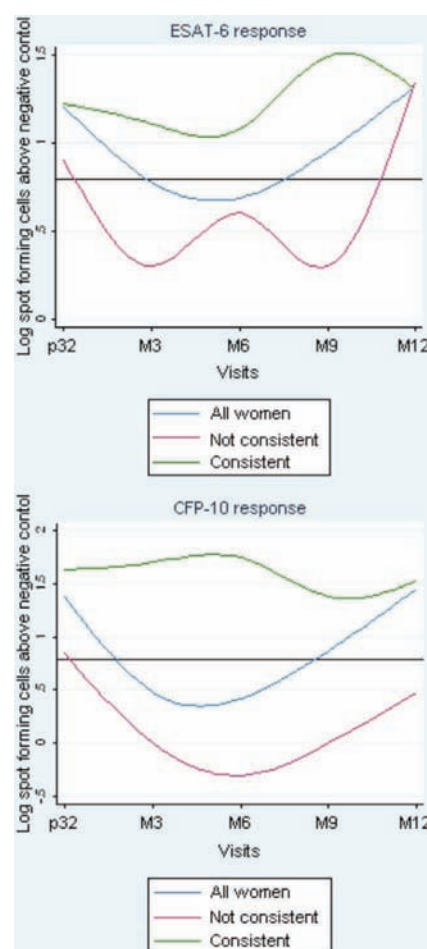
Figure Median log10 ESAT-6 and CFP-10 responses in all women, women with consistently reactive responses through follow-up and in women with fluctuating responses (not consistent) through follow-up. Horizontal black line represents the cut off value for a reactive T-SPOT.TB response.

specimens from 3, 6, 9 and 12 months postpartum to assess consistency of responses. None of the women had active TB at pregnancy or during follow-up.

Results: Among 18 women with 72 serial assays, 63 (87.5%) assays were valid. In serial testing, 9 (50%) women had 2–4 subsequent time-points tested all of which remained positive, 3 (17%) women had 3–4 subsequent time-points tested, none of which were positive and 6 (33%) women had 3–4 subsequent time-points tested that fluctuated between reactive and non-reactive responses. Women with consistently reactive results had greater mean IFN-γ response over all visits compared to women with postpartum changes in results (reactive to non-reactive and vice versa) (log10ESAT-6 spot forming cells (SFCs): 1.5 vs. 0.71; $P = 0.006$; log10CFP-10 SFCs: 1.55 vs. 0.33; $P < 0.001$). IFN-γ levels in women with changes in results were closer to the cut-off for a reactive response (Figure). Average rate of change in IFN-γ response per 3 month intervals was −0.01 (95% confidence interval [CI] −0.09–0.07; $P = 0.81$) and 0.02 (95%CI −0.07–0.10; $P = 0.73$) for log10 ESAT-6 and CFP-10, respectively and was not associated with baseline CD4 or specific postpartum time-point.

Conclusion: HIV-1 infected pregnant women with highly reactive IGRA responses retained reactivity whereas those with initially weak responses fluctuated between reactive and non-reactive responses. IFN-γ magnitude was not significantly altered suggesting minimal influence of hormonal or immune changes in pregnancy/postpartum on IGRAs, which supports potential utility of IGRAs during this period.

FA-101305-14 Treating TB-HIV: 6m vs. 9m. 8 years experience from Peru

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Background: The prevalence of TB-HIV is <2% among TB patients in Peru. About 80% of them are in Lima-Callao. Until 1995 they received 2RHZE/4 (RH)2 full supervised for health workers in both phases. Since 1996 until 2006, the regimen was changed to 2RHZE/7 (RH)2. Since 2006 again they received 6 months regimen, full supervised (since May 2004 HAART was implemented).

Design: Retrospective comparative cohorts of treatment of TB-HIV with 2RHZE/4 (RH)2 vs. 2RHZE/7 (RH)2 regimens, full supervised.

Results: 1220 patients were included in the cohorts, from January 2001 to December 2008. 105 patients were excluded. All of them were recruited from public hospitals and health establishments. Source: TB-Registry (cohort report). Risk of failure (6 m vs. 9 m): OR = 0.65, 95%CI 0.26–1.58, $P = 0.311$; risk of death: OR = 0.59, 95%CI 0.44–0.78, $P = 0.000$;

Table   Comparative cohorts TB-HIV 6m vs. 9 m, Peru

Year	Total	Cure %	Fail %	Deaths %	Default %	Transf %
a) 2001–2006	815	53.8	2.4	35.6	7.0	1.6
b) 2007–2008	405	62.7	2	25.3	9.3	0.8

a) 2RHZE/7R2H2
b) 2RHZE/4R2H2

risk of default: OR = 1.28, 95%CI 0.8–2.0, $P = 0.280$.

Conclusion: Between 2001 and 2008, the cure rate has increased from 53.8% to 62.7%, there was no significant differences respect of failure nor default proportion. Six months regimen was associated with significant lower death rate, probably due to HAART access, not necessarily to TB treatment.

FA-101465-14 The role of abdominal ultrasound in the diagnosis of tuberculosis in Rwanda

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Background: In HIV-prevalent settings smear-negative pulmonary and extra-pulmonary tuberculosis (TB) are common and pose diagnostic difficulties. Specific findings on abdominal ultrasound may speed up this diagnosis.

Objectives: To evaluate the role of abdominal ultrasound in the diagnosis of smear-negative pulmonary or extra-pulmonary TB.

Methods: Post hoc description of abdominal ultrasound findings from an observational cohort of adults treated for TB at the Internal Medicine department of the Kigali University Hospital from May 1, 2008–February 1, 2009. Associations between a diagnosis of TB and suggestive abnormalities such as abdominal lymphadenopathy, splenic nodules and effusions were explored.

Results: Of the 259 patients enrolled (mean age 35 years, 172 HIV-infected, mean CD4 cell count 166/mm³), 180 (69%) had smear-negative and/or extra-pulmonary TB. Of those, 132 (73%) had a positive HIV-serology. Abdominal ultrasound was performed in 146 (77%) smear-negative and extra-pulmonary TB cases. Suggestive abnormalities were found in 99 (68%) patients: enlarged intra-abdominal lymph nodes (55), hypoechoic nodules of the spleen (22) and effusions (ascitic 39, pleural 24, pericardial 15). Abdominal ultrasound was the only positive diagnostic element in 33 (17%) cases. HIV infected patients were more likely to have abdominal lymphadenopathy and splenic nodules (respectively, $P = 0.002$ and $P = 0.011$). The latter was also associated with disseminated TB ($P < 0.0001$).

Conclusion: Although not recommended by the WHO, abdominal ultrasound is widely used by clinicians and commonly contributes to the diagnosis of TB in our setting. It was the only diagnostic element in almost a fifth of the patients. Although a more in depth analysis is required, our data support a broader use of abdominal ultrasound in the diagnosis of TB in similar settings.

TB PROGRAMME IMPLEMENTATION: GRASS ROOTS AND TREE TOPS

FA-101295-14 The effectiveness of facility-based and community-based care for tuberculosis in 10 districts of Ethiopia

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Aim: Convenient and high quality tuberculosis care is important to control tuberculosis in high burden countries like Ethiopia. Access to health facility-based tuberculosis care is limited to rural patients. We therefore tested the effectiveness of two additional patient-convenient care options.
Methods: New adult smear-positive pulmonary patients were randomly assigned prospectively into 3 care options: health facility-based health worker (179 patients), CHWs (179) and self-treatment after month one of treatment in health facilities (179). In addition, 131 new adult smear-negative pulmonary patients were assigned into each of the three arms. The study was conducted in public health facilities in 10 districts with DOTS tuberculosis programme. The quality of tuberculosis care and district control programme management was strengthened as per the recommended control standards. All patients received daily standard 8 month treatment regimens. Separate analyses for both diagnoses were conducted on the basis of intention-to-treat.
Results: The treatment completion rates for smear-positive cases under health facility-based health worker, CHW and self-treatment groups were 88%, 88% and 92% respectively. There was no significant difference in cure rates among smear-positive patients assigned to the health worker group and those in the self-administered group (−2.2% difference; 95%CI −8.5–4.2) or the CHW group (−0.5% difference; 95%CI −6–7.4). The treatment completion rates for smear-negative patients were also similar across the three groups with no significant difference between the three treatment groups.
Conclusion: A convenient and good quality tuberculosis care gives equally high treatment success rates after the one month initiation phase in health facilities. The reduced period of daily care and village based care by CHWs made treatment more accessible and appropriate for patients.

FA-100029-14 Simple educational interventions improve compliance with smear-negative TB diagnostic guidelines

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Background: In low resource settings, diagnosis of smear negative pulmonary tuberculosis (PTB) relies on clinical algorithms. Failure to adhere to these may lead to diagnostic delay or missed diagnoses on one hand, or unnecessary drug treatment risking toxicity, interactions and selection for resistant strains on the other.
Methods: An audit undertaken in 2007 and 2009 on the Malawi National TB Program (NTP) guidelines for diagnosis of smear negative PTB. Following initial data analysis, simple educational interventions were undertaken. Firstly, interns in the Department of Medicine were regularly reminded of national guidelines. Secondly, all patients requiring admission for TB treatment were medically assessed prior to starting therapy, rather than simply being admitted to the TB ward as frequently happened previously. Thirdly, regular informal meetings with the TB officers were introduced, emphasising the need to comply with guidelines. Finally, education was provided regarding screening for TB prior to introducing anti-retroviral therapy, and the need for HIV testing in all patients with a diagnosis of TB. This was done through the regional HIV meeting, and at regular teaching meetings throughout the 2 years between the data collections.
Results: Adherence to NTP guidelines in the diagnosis of smear negative PTB improved between 2007 and 2009. More patients were symptomatic for greater than three weeks ($P = 0.041$) and fewer patients received multiple courses of empirical antibiotics ($P < 0.0001$), reducing diagnostic delay. A marked improvement in both the number of patients testing for HIV ($P = 0.001$), and a willingness amongst patients with unknown HIV status to test were noted.
Conclusion: Simple and brief educational interventions can improve compliance with NTP guidelines in diagnosis of smear negative TB at a teaching hospital in Malawi. Further work is required to see if these

Criterion	2007 (%)	2009 (%)	*P* value
3 or 4 criteria met (compared to 0–2)	80.2	95.6	0.006
Cough >3 weeks	81.5	92.2	0.041
3 sputum samples sent and results recorded	91.4	95.6	0.353
1 appropriate course of antibiotics (cf ≥2)	13.6	55.6	<0.0001
CXR consistent with PTB	72.8	81.1	0.208
HIV status known	75.3	93.3	0.001
HIV status unknown, unwilling to test	8.6	0.0	0.09

same simple interventions can improve compliance at district hospital levels.

FA-100832-14   A breakthrough for quality assurance of chest radiography with a simple quality assessment tool

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Background: The quality of chest radiography (CR) is essential for accurate diagnosis of smear negative pulmonary TB and all patients with lung diseases. However, no standardized quality assurance (QA) activity has been developed yet in most countries. Given this worldwide need of improvement of the quality of CR, TBCAP developed an assessment tool for resource-limited settings. The assessment tool simply categorizes the quality of CR into 4 different stages such as; E, G, F and P, based on 6 quality factors. TB-CAP conducted two 5-day international trainings in Cambodia and Kenya in 2009.
Methods: The 34 participants from 14 countries were trained and acquired the basic knowledge on QA of CR and how to use the assessment tool. As a part of the training, they made a plan for a situation analysis of the quality of CR in their countries and were assigned to conduct an assessment after return.
Results: The situation analysis included the assessment of 50 CR films, 5 films in 10 different health facilities. Five countries in Asia and three countries in Africa completed the assignment. The results from eight countries show that the quality of CR in their reports varies widely with between 90% of E or G to more than 90% F or P. Data on equipment and X-ray factors used in the assessed facilities was reported from six countries. The report shows that only 10 health facilities out of 59 apply more than 100kV which is dominant as a standard technique for CR in developed countries. Moreover, in 35 health facilities out of 59, average examination number of CR was less than 20 patients per day. The data from the reports implies that insufficient numbers of patients were examined with lower kV technique which may produce low quality of CR.

Conclusions: The TBCAP tool for the quality assessment of CR is a valuable and simple tool for training in basic QA of CR. The experiences gained from this project should be further promoted under the leadership of the Ministry of Health.

FA-100110-14   Community drug distribution points reduce antiretroviral therapy loss to follow-up dilemma

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Background: Accessibility difficulties in getting to the clinic and transport problems are some of the factors causing loss to follow-up after initiation of antiretroviral therapy (ART) in Africa, which is a considerable obstacle for service providers to understand the effectiveness of treatment outcome. TASO Tororo implemented the CDDP model of ART delivery with the objective of reducing loss to follow-up; improve accessibility and retention of clients on ART program.
Description: Clients who met national eligibility criteria were enrolled on ART; they received medical review at 2 weeks, 6 weeks, 8 weeks and drug refills at the facility or ART satellite clinics in the community. They were then assessed for stability on ART and given appointment for the subsequent two months refills by Field Officers (HIV/AIDS counselors with basic training on ART) at a CDDP nearest to them. Community ART Support Agents (CASAs) did roll calls and followed up on those who did not turn up on appointment in liaison with Field Office.
Results: In 2008 out of 2115 active client enrolled on ART (female 1325, male 691 and 135 children <18 years) in TASO Tororo, 1734/2115 (82%) received ART refills and monitoring at the CDDPs with 95.5% of them having adherence levels >95%. Only 22/2115 (1.0%) were lost to follow-up, 1734 monitored jointly with Field Office for adherence. Clients had the opportunity to sharing experiences and support each other on issues related to side effects, adherence, family planning and condom use, there was a strong enhancement on disclosure, adherence, and community awareness, reduction on stigma and discrimination and optimal use of limited resources.
Conclusion: The CDDP model of ART delivery has proved effective not only in countering loss to follow-up but also improved ART accessibility, adherence, client retention and optimizing limited resources.

FA-101352-14   The causes of ATBM shortages in GFATM and GDF supported countries and how to avoid it in the future

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Methods: A regional survey was done during the GDF/ WHO field visits in 15 of GDF supported countries, 12 of them are supported by GFATM. 76 Directors of the pharmacy depts. at MOH, NTP staff were interviewed; the questionnaire endorsed GDF/ WHO questionnaires about the availability of the Anti-TB medicine (ATBM) at the central /district level, causes of shortage of ATBM at all levels in these countries, how countries were managing their ATBM supply system, how the shortage took place despite the era of these high quality initiatives, what are possible causes behind, how (WHO & countries) have (tried to) manage the shortage, and what is the possibility for having no future shortage of ATBM.

Results: Usable responses were received; among 15 of GDF supported countries; 20% of them, the shortage was due to noticeable decrease in the political commitment towards ATBM funding, 13.3% was due to unplanned switching to 6 months regimens in countries which were working on the 8 months regimens, 26.6% was due to a delay of funding of ATBM, in the 33.3% of the 12 GF supported countries. Significant increase in the GDF lead time of ATBM orders was noticed as a result of the above reasons in 20% of the surveyed countries. The last 20.1% was due to different reasons; like delay in port clearance, lab analysis delay, etc. For the future no shortage of ATBM, it was suggested to; establish a new channel of working between GDF/ GFATM and countries in the Drug supply system, to continue support the regional partnership with some societies in the region which overcame the shortage, working on the rational use of ATBM and WHO Pre-qualification for more GDF/WHO pre-qualified suppliers, working with countries to improve their capacity building and Drug management cycle.

Conclusion: GFATM and GDF should establish a new channel with countries to improve the drug supply system. WHO should continue support the regional partnership to avoid and /or over come any future shortage.

FA-100455-14   Development of PPM installation package for expanding DOTS in the Philippines: a 5 year experience

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Background: The private sector in the Philippines was previously a large, untapped resource in TB control. The 1997 TB Prevalence Survey revealed that a significant proportion of patients seek the consultation of private physicians. However, not all of them adopt the DOTS protocol. More so, variations in the treatment regimen increase the patients' risk of treatment failure, MDR-TB and death. A strategy is necessary to involve them in TB control.

Intervention: A PPMD Installation Package is designed to engender commitment from private sector. It is a step by step process aimed at establishing units that will provide quality DOTS services. The package includes advocacy and capacity building tools and mechanisms. A national and 16 regional coordinating committees were established to oversee package implementation. With funding from the Global Fund, the package was introduced in 7 areas in 2004, additional 21 in 2005, 42 in 2006, 47 in 2007 and 52 in 2008 for a total of 169 areas.

Results/lessons learnt: Strategically serving about 36 million Filipinos, the PPMD contributed 6% to CDR in 2008 and achieved 90% treatment success rate. From 2004 to 2008, 2912 private physicians were trained and encouraged to comply with NTP guidelines. As of 2008, the initiative has enabled 36 870 patients to have access and receive quality DOTS treatment, out of which 15 892 were new smear (+) cases. Coordinating structures played lead role in ensuring that plans and targets are met. Involvement of highly motivated champions and advocates, strong NTP and an effective monitoring system are keys to the success of the initiative. The package is cost-effective in areas with critical mass of private practitioners.

Conclusion/key recommendation: The package enables rapid scale up of PPMD expansion significantly contributing to the NTP. Local coordinating structures to implement the package should be expanded and sustainability should be ensured for continuity of DOTS service.

FA-101546-14   Controlling TB in prisons against imprisonment conditions—a lost case? An experience from Cameroon

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Background: Tuberculosis (TB) is recognised as a major public health problem in prisons of sub-Saharan Africa. In Cameroon, major prisons have become diagnosis and treatment units within the National TB Control Programme (NTCP). This study aimed to assess the effectiveness of routine TB control activities by determining the prevalence of undetected pulmonary tuberculosis (PTB).

Methods: In 2009, a PTB case finding survey was undertaken in the Central Prison of Yaounde (CPY), Cameroon. All prisoners with cough for ⩾1 week's

duration were screened by sputum-smear microscopy. Smears were sent to the national reference laboratory for culture and drug sensibility testing (DST). Voluntary counselling and testing for HIV were offered to all inmates.

Results: Among 3219 inmates screened, forty (1.2%) inmates identified with PTB had been missed by the prison TB control programme. PTB was positively associates with severe crowding, a low body mass index, and anterior TB treatment. Four in 40 (10%) inmates were TB-HIV coinfected. The DST of three inmates revealed resistance against anti-tuberculosis drugs.

Conclusion: Despite a well performing TB control programme in the CPY, the number of undetected PTB cases remains unacceptably high. It is doubtful whether TB transmission can be controlled under confinement conditions like in the CPY.

FA-100511-14   Tuberculosis and smoking among patients entering a DOTS program in Rio de Janeiro city, Brazil

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Background: There are few studies on the prevalence and the impact of smoking among TB patients in Brazil. We evaluated the prevalence of smoking among TB cases entering a clinic-based DOTS program in Rio de Janeiro city, Brazil and compared socio-demographic, clinical characteristics and treatment outcomes among smokers and non-smokers.

Methods: This study was part of a larger study on DOTS implementation. Newly diagnosed TB patients attending 3 health centers from November 2000 to December 2004 were included. A structured interview including smoking experience was given at enrollment.

Results: Among 730 patients included, 381 (52%) reported a history of ever smoking. Smokers were older (median age = 39 years) than non-smokers (28 years), equally likely to be male (60% in each group), and less educated (16% vs. 33% had >8 years of education. TB smokers had a higher proportion of alcohol consumption (41% vs. 21%), injection drug use (8% vs. 3%), HIV co-infection (10% vs. 6%; all $P <$ 0.05). TB smokers also had a higher proportion of previous TB (26% vs. 20%), pulmonary TB (94% vs. 89%), cavitary lesions (53% vs. 45%), positive sputum smear (85% vs. 73%) and treatment default (17% vs. 10%). In the logistic regression, treatment default was associated with ever smoking (aOR 2.3; 95%CI 1.4–3.7), age (aOR 0.98, 95%CI 0.96–0.99) and past TB (aOR 2.82 95%CI 1.78–4.47).

Conclusions: The prevalence of smoking among TB cases was much higher than in the adult population in Brazil (16%) and smokers were more likely to default on TB treatment. Smoking prevention and cessation efforts should be included as activities of a TB control programs.

FA-100474-14   Does contact tracing as part of intensified case finding increase TB case-finding in Western Kenya?

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Background: Identification of new infectious cases is the highest priority in TB control programs yet presents the greatest logistical challenge. Cough monitors (CMs) based in Eldoret, Kenya perform Intensified Case Finding (ICF) with a combination of community sensitization, symptom screening, and in-field sputum collection. While CMs are encouraged to do contact tracing (CT) of smear-positive patients, no formal CT training or evaluation has been instituted. The contribution of CT to other ICF activities remains unknown in this setting.

Methods: 49 health care sites were cluster-randomized by district according to urban or rural location and prior rates of smear-positivity. Sites were instructed to perform either structured contact tracing or 'business as usual.' All CMs received identical data collection forms; CMs at CT sites received further training on conducting contact tracing to identify infectious cases in households. Data were collected from CM forms and facility lab registers. Primary outcomes: 1) rate at which smears were performed (smears per unit time), 2) rate of smear-positives (per unit time), and 3) yield of smear (smear-positives over all smears)

	Contact tracing sites	Non-contact tracing sites
All suspects screened with sputum	669	1005
Smear-positive index cases	121	142
Households contacted for contact tracing	65	NA
Households that accepted contact tracing	52	NA
Persons living in index case households	141	NA
Avg. age of household members (years)	20.0	NA
Contacts screened with symptom questionnaire	72	NA
Contacts with sputum collected	39	NA
Smear-positive contacts	2	NA

per site. The main measures for comparison were the ratios of these rates and yield in the follow-up period to the baseline. Poisson regression, adjusted for cluster randomization, was used to calculate relative rate and yield ratios for CT vs. control sites.

Results: Data from the initial 3 months of a planned 12-month study are analyzed. The relative rate ratio for all smears performed, comparing CT to control, was 1.15 (95%CI 1.05–1.26); the relative rate ratio for smear positives was 1.04 (0.78–1.38); the relative ratio for smear yield was 1.17 (0.72–1.88). See Table for a summary of CT investigations.

Conclusion: Preliminary data indicate that CT added to existing ICF activities may not augment TB case-finding in the high-burden setting of Western Kenya.

FA-100733-14   Natural ventilation in traditional Zulu homes in an area of South Africa with high rates of M/XDR-TB

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Background: Primary transmission of drug-resistant tuberculosis (DR-TB) has been responsible for the epidemics of MDR- and XDR-TB in rural Tugela Ferry, South Africa. Nosocomial transmission has been convincingly demonstrated, and limited observational and mathematical modeling studies suggest an increasing proportion of transmission will occur in household and other community settings. Natural ventilation in hospitals can decrease risk of TB transmission, but there is no information about transmission risk and reduction within traditional rural African homes.

Objective: To investigate air movement in traditional Zulu homes by measuring air changes per hour (ACH), and to estimate the effect of natural ventilation on the risk of TB transmission in this setting.

Methods: We are evaluating a variety of traditional Zulu homes, measuring their structure (e.g., room volume, window/door area, thatched/metal roof) and ambient air (e.g., temperature, wind speed). Using a CO_2 tracer gas technique, we measure ventilation under a range of conditions (e.g., all openings closed, windows open, windows and door open) to calculate ACH for each. Risk of TB infection is calculated using an adapted Wells-Riley model.

Results: Preliminary results from this ongoing project show that when all windows and doors are closed, ventilation is poor (median 2.9 ACH, range 1.0–16.4; Table). Air flow improves with opening of windows (median 15.5 ACH, range 8.7–36.1), and further when the door is opened (median 25 ACH, range

Home	Room volume (m³)	Ventilatory spaces (m²) Windows	Door	Extra spaces	Cross-ventilation?	Closed windows/door ACH	% TB risk*	Windows open ACH	% TB risk*	Door + windows open ACH	% TB risk*
Round, thatched roof	70.7	0.7	1.2	0.0	Yes	1.7	47.7	9.5	10.9	22.7	4.8
Round, thatched roof with space between top of wall and roof	108.5	0.8	1.6	2.1	Yes	16.4	4.3	21.5	3.3	40.2	1.8
Rectangular, metal roof, large room	45.4	2.7	1.7	0.0	Yes	1.0	82.0	36.1	4.6	27.3	6.1
Rectangular, metal roof, small room	24.9	0.4	1.6	0.0	No	4.0	54.3	8.7	30.3	21.7	13.4
Median						2.9	51.0	15.5	7.8	25.0	5.5

*Risk = Risk of TB transmission based on Wells-Riley model: C = S(1 − e-Iqpt/Q) where: C = number of new cases; S = number of susceptible individuals exposed; e = base of natural logarithms; I = number of infectors; q = number of infectious "quanta" produced per hour by infectors; p = pulmonary ventilation rate of susceptible individuals; t = exposure time (hours); and Q = absolute room ventilation (m3/h). We make the following assumptions based on available information about TB transmission and the community surrounding Tugela Ferry: S = 2 susceptible individuals; I = 1 infector; q = 13 infectious quanta per hour; p = 0.6 m3/h; t = 10 hours exposure time.

21.7–40.2). These improvements in ACH decrease the risk of TB infection by household contacts from 51% to 7.8% and 5.5%, respectively.

Conclusions: These preliminary data indicate that simple improvements in natural ventilation can increase the ACH in traditional Zulu homes and may decrease risk of DR-TB transmission to other household members. Natural ventilation should be encouraged along with other infection control measures in communities with high TB and HIV prevalence.

CLINICAL RESEARCH AND PROGRAMME IMPLEMENTATION IN CHILDHOOD TB

FA-101062-14   Diagnostic utility of the QuantiFERON Gold In-Tube assay in pediatric intrathoracic TB patients

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Aims: To assess the diagnostic utility of the Quanti-FERON Gold In-Tube (QFT) assay and the tuberculin skin test (TST) in children with intrathoracic TB.

Setting: Tertiary care hospital, New Delhi, India.

Methods: Children with intrathoracic TB underwent

Table Comparison of the QFT and TST tests in pediatric intrathoracic TB

	TST	
	⩾10 mm	⩽10mm
Primary complex (*n* = 38)		
QFT		
Positive	35 (6)*	0
Negative	3 (0)*	0
Kappa statistic = 0.0; (95%CI –1.086–1.086); agreement between tests = 92% (poor).		
Progressive disease (*n* = 76)		
QFT		
Positive	56 (18)*	7 (4)*
Negative	8 (2)*	5 (1)*
Kappa statistic = 0.3 (95%CI 0.043–0.608); agreement between tests = 80.3% (fair).		
Pleural effusion (*n* = 27)		
QFT		
Positive	19 (5)*	3 (1)*
Negative	3 (1)*	2 (2)*
Kappa statistic = 0.264 (95%CI –0.256–0.783); agreement between tests = 78% (fair).		

* Patients who were AFB smear and/or culture positive.

examination with the QFT and TST (5TU-PPD) tests prior to initiation of TB treatment. TB was defined radiologically (2 independent experts) and/or bacteriologically (smear and/or culture of mycobacteria from induced sputum and/or gastric aspirates).

Results: 141 patients (median age 109 months; IQR 60–144) were included. Radiologically, 38 (27%) had primary pulmonary complex (PC), 74 (53%) progressive disease (PD); 27 (19%) had pleural effusion (PE). 95 (67%) received BCG vaccination; 50 (35.5%) had a contact history with an adult TB patient. The weight for age was <−3z in 60 (43%). *M. tuberculosis* was identified in 40 (29%) children (smear and/or culture positive). The TST was positive in 124 (88%) and the QFT was positive in 120 (85%). Discordant results between the TST and QFT tests were obtained in 24 children (McNemar's test *P* = 0.541) (Table). QFT positivity rate correlated with induration of TST [58.5% for TST < 10 mm, 84.9% for TST 10–19 mm and 94.1% for TST > 19 mm (*P* = 0.004)]. Mycobacterial yield, nutritional status, BCG status, serum zinc and copper levels were similar between children positive by either TST or QTF.

Conclusion: The TST and QFT had comparable performance in children with intrathoracic TB. The agreement between the two tests ranged from poor (PC) to fair (PD and PE) in intrathoracic pediatric TB patients.

FA-101419-14   Can we reduce susceptibility to TB in children with HIV?

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Rationale: Children with HIV remain susceptible to TB, even when receiving anti-retroviral therapy (ART), but could gain additional protection from safe, more efficacious TB vaccines. However, there is little information regarding immunogenicity of mycobacterial antigens in this group.

Objectives: 1) To assess the impact of ART on the ability to restrict growth of *M. tuberculosis* in an in vitro whole blood model; 2) To characterise mycobacteria-specific T cells in HIV-positive children in responses to antigens assessed for inclusion into novel TB vaccines.

Methods: Whole blood was collected from HIV-infected children (*n* = 30) prior to commencing ART and incubated with reporter-gene tagged M.Tb H37Rv (lux) in vitro. Mycobacterial growth was measured in 3-monthly intervals following introduction of ART and correlated with longitudinal recovery of CD4 T-cell numbers and function during the first 12 months on ART. Additional samples were stimulated with Ag85B, TB10.4 and control antigens. Intracellular cytokine production and memory phenotype of antigen-specific CD4 and CD8 T cells were determined using 8-colour flow cytometry.

Results: There was significant increase in the ability to suppress growth of M.Tb in vitro following introduction of ART (*P* = 0.0085), correlating with increase in CD4 T cell numbers (r = 0.75, *P* = 0.001). CD4 and CD8 T cell responses to AG85 and TB10.4 were detectable in most children, but varied in magnitude. CD4 T cells secreting IFN-γ, IL-2 or both expressed a CD45RA-CCR7-CD27+/− effector phenotype. CD8 T cells secreted mostly IFN-γ and expressed a CD45RA-CCR7-CD27- or CD45RA+CCR7-CD27- effector phenotype.

Conclusions: Introduction of ART leads to sustained improvement of anti-mycobacterial immune responses in this in vitro model. Mycobacteria-specific T cell responses deemed protective are detectable also in HIV-infected children and could be further enhanced by new TB vaccines currently in clinical trials.

FA-100491-14   Ethionamide pharmacokinetics in children with tuberculosis: preliminary results

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Introduction: Ethionamide (ETH) is a frequently used second-line antituberculosis drug in childhood tuberculosis. Due to a lack of paediatric data, ETH dose recommendations in children are derived from adults.
Aim: To determine the pharmacokinetic parameters for ETH in children on antituberculosis treatment including ETH.
Methods: ETH serum levels were prospectively assessed in 31 children, mean age 4.25 years. Children were divided into equal groups according to age (0–2 years, 2–6 years, 6–12 years). Within each age group half received rifampicin (RMP) and half did not. Following an oral dose of ETH (15–20mg/kg), serum samples were collected at 0, 1, 2, 3, 4 and 6 hours and assayed by high-performance liquid chromatography. Maximum serum concentration (Cmax), time to Cmax (tmax) and area under the time-concentration curve from 0–6 hours (AUC0-6) were calculated.
Results: Mean Cmax for all age groups was above the suggested therapeutic serum concentration of 2.5 μg/ml (mean = 4.14 μg/ml, range 1.48–6.99 μg/ml) and reached within two hours (mean tmax 1.29h, range 0.87–2.97 h). Mean Cmax differed significantly between children with and without concomitant treatment with RMP in children >6 years ($P = 0.047$) as well as between those >6 years and those 2–6 years when treated with both ETH and RMP ($P = 0.047$). There was no significant difference regarding tmax and AUC0-6 between the study groups. Elimination occurred faster in children <2 years (t ½ = 1.1h) than in children 6–12 years (t ½ = 1.5h).
Conclusion: ETH at dosage of 15–20mg/kg leads to serum concentrations above the therapeutic level in children younger than 12 years irrespective of concomitant treatment with RMP. Younger children eliminate ethionamide faster than older children.

FA-100656-14   An ounce of prevention: treating MDR-TB contacts in a resource-limited setting

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Background: Persons exposed to multidrug-resistant tuberculosis (MDR-TB) should be evaluated and considered for treatment for latent TB infection, which could prevent TB disease and mitigate an outbreak. During two coincident MDR-TB outbreaks in Chuuk, Federated States of Micronesia, a setting with geographic barriers and limited resources, more than 200 persons were exposed to at least one of 19 contagious patients during December 2007–January 2009.
Intervention: Household members, healthcare workers, and others with contact to an MDR-TB patient were screened with a tuberculin skin test (TST), chest radiograph, symptom review, and sputum microscopy and culture if TB disease was suspected. Treatment by directly observed therapy (DOT) for latent infection (presumed MDR) was offered to contacts with a TST induration of ⩾5 mm and no evidence of TB disease. Daily treatment, based on the drug susceptibility pattern from the presumed source case, was a fluoroquinolone and ethambutol, a fluoroquinolone and ethionamide, or a fluoroquinolone alone.
Results: The 19 MDR-TB patients had 205 contacts, of whom 124 (60%) had latent infection. Four were medically ineligible for the treatment regimen, and 10 (8.3%) refused treatment. Of 110 patients who started treatment, 92 (84%) completed 12 months under DOT; 6 (5.5%) of the 110 who started reported side effects that caused treatment interruptions. As of March 2010, MDR-TB disease had not developed in any of the contacts receiving treatment for latent infection under DOT.
Conclusions and key recommendations: Despite remarkable challenges, the Chuuk TB program successfully implemented DOT for treating latent MDR-TB infection, with an 84% completion rate and good tolerability of drug regimens. Completing treatment for latent MDR-TB infection can be accomplished in resource-limited settings and may be a promising step in controlling MDR-TB.

FA-100701-14   Utility of chest radiograph in screening HIV-infected children for tuberculosis

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Background: TB-HIV co-infection in children leads to significantly increased morbidity and mortality. Diagnosis of TB in HIV-infected children remains very challenging, especially in resource-poor settings. Evaluation of available low cost tools including chest radiograph to improve diagnosis at screening is needed.
Methods: From March to December 2009, participants in a prospective cohort study at Family AIDS Care and Education Services (FACES) evaluating TB in HIV-infected children in Nairobi and Kisumu,

Kenya age 6 weeks to 14 years were screened for active pulmonary TB. Screening included TB score chart, tuberculin skin testing, and CXR regardless of symptoms. Training on CXR interpretation using a standardized reading form was provided. TB was diagnosed according to WHO criteria. Analysis was performed using dichotomous tables and calculating sensitivity (sens), specificity (spec), positive predictive value (PPV), and negative predictive value (NPV).

Results: Thirty-two (9.8%) TB cases were identified out of 325 children screened. Of those screened, 31% had an abnormal CXR. Abnormal CXR were found in 81% of children diagnosed with active TB but only 26% of those without. An abnormal CXR had a sens = 81%, spec = 74%, PPV = 26%, and NPV = 97% for TB. Abnormal findings included hilar lymphadenopathy (27%), airspace abnormality (13%), miliary appearance (<1%), airway compression (0) and airway displacement (0). The findings with the highest specificity and NPV for TB were hilar lymphadenopathy (spec = 77%, NPV = 93%) and airspace abnormality (spec = 92%, NPV = 93%).

Variable	Sens. %	Spec. %	PPV %	NPV %
Abnormal CXR, $n = 101$	76	84	31	97
Hilar lymphadenopathy, $n = 78$	43	90	30	94
Airspace abnormality, $n = 29$	29	94	32	93
Miliary appearance, $n = 2$	9	100	100	92

Conclusions: A large proportion of children with HIV have abnormalities on routine CXR. A normal CXR, particularly, absence of hilar lymph nodes and airspace abnormality are highly specific in ruling out TB. Routine screening of HIV-infected children using CXR is helpful in identifying those with active TB. Training of clinical staff to interpret CXR would improve screening and early diagnosis of children with TB.

FA-100842-14   Contact screening of children of DR-TB patients in Karachi, Pakistan

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Background: Tuberculosis is one of the leading causes of morbidity and mortality across all age groups especially in developing countries 1). Among household contacts, those who are very young and those with immunodeficiency states are at increased risk of acquiring infection from the index case. 2) Little is known about the long-term outcome of children in contact with MDR adult pulmonary TB cases.
Aims: To study the prevalence of tuberculosis infection and LTBI among children in household contact with adults having drug resistant pulmonary tuberculosis.

Methods: Children under 15 years of age in direct daily contact with adults with drug resistant tuberculosis who were registered with and being treated at the Indus Hospital Karachi DOTS-Plus program from January 2008 to January 2010, were actively evaluated at the Indus Hospital Infectious Disease Clinic.
Results: 117 children <15 years of age in contact with 33 adults with drug resistant tuberculosis (DR-TB) were evaluated. 26/117 (22%) children belonged to the high risk under 5 year age category, 46% of these children were severely malnourished and had a suspicious chest X-ray. 4/117 (3.4%) contact children were found to have active disease. 36/84 (43%) of contact children had a positive tuberculin skin test 26/117 (22%) had a >15mm TST reaction, 80% of these children did not have a BCG scar.
Conclusion: We found that 43% (36/84), of the contact children had a positive TST (which is higher than that reported from a similar Indian study) (4) 3.4% of contact children were found to have active pulmonary disease. Children in contact with adult patients are at the highest risk of getting infected and progressing to active disease. Contact screening is important for early detection of transmission of infection and should be a part of the National TB program in Pakistan.

FA-100794-14   Tools to improve case finding of pulmonary tuberculosis in HIV-infected children

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Background: Children with both TB and HIV have 20-fold increase in TB incidence and 3–6 times higher mortality. Emphasis has been placed on routine screening for TB in HIV-infected adults but has lagged behind in children. Approaches aimed at improving case finding in this vulnerable population are needed.
Intervention: We developed an approach to improve case finding of TB in HIV-infected children age 6 weeks to 14 years as part of a prospective cohort study determining TB incidence and prevalence in this population in Kenya. Training on TB diagnosis in children, chest radiograph (CXR) interpretation, and tuberculin skin testing (TST) were given to all staff at three Family AIDS Care and Education Services (FACES)-supported clinics in Nairobi and Kisumu. All children underwent TB screening including a symptom based checklist, TST, TB score chart, and CXR regardless of symptoms. TB was diagnosed according to WHO criteria. Prior to implementation of this intervention, TB screening was performed only if a clinician suspected TB.

Outcome: Of the 485 children screened, 43 (8.9%) had active TB. Of these, 60% were female with a median age of 5.8 years (1.3–14years), majority were in WHO stage 3 with a median CD4% of 25.8% (9.5–51%). The median TB score was 7 (−1 to 10) as compared to median score of −1 in those without TB. Children with TB were more likely to have positive TST (44% vs 11% $P < 0.001$) and an abnormal chest X-ray (78% vs 27% $P < 0.01$). For children without active TB 85% were on HAART compared to 70% of those with active TB. Although a high number of children overall were on HAART, children on HAART were less likely to develop PTB ($P < 0.05$).

Conclusion: This intervention demonstrates that a high number of TB cases in HIV-infected children can be identified. Using low-cost, available tools including score charts, CXR, and TST, more TB co-infection can be identified. Emphasis on routine screening for TB in children infected with HIV/AIDS is needed.

FA-101094-14   Increasing childhood TB referral and detection in rural Bangladesh

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Background: In Bangladesh a recent estimate suggests only one in six children with TB are currently detected by the NTP DOTS programme. The objective of this study was to increase referrals of children with suspected TB as well as to increase the diagnosis of referred cases at 18 Damien Foundation Microscopy Centres (MCs) by using the WHO score chart.

Design/Methods: In this prospective community based intervention study, community agents who usually refer TB cases were oriented and motivated to refer children with suspected TB in the catchment area of 18 randomly selected intervention MCs. Tuberculosis and Leprosy Control Assistants (TLCAs), were trained to administer the WHO Child TB score chart as well as the Mantoux Test which is an essential parameter of the chart. After training and 12 months of screening and referral, an assessment was carried out to see if the number of referrals and TB case detection in children had changed in the intervention MCs compared to 18 other matched controlled MCs.

Results: After 12 months of screening and referral, a preliminary assessment shows a fourfold increased diagnosis of childhood TB in intervention centres compared with centres where there has been no such intervention. This increase was validated with qualitative and quantitative assessments of the processes.

Conclusion and recommendations: TB detection can be simply integrated into existing NTPs worldwide through training. The training and BCC materials developed for this research project can be shared in the process of scaling up.

POSTER DISCUSSION SESSIONS

TB-HIV EPIDEMIOLOGY

PC-100341-14   Prevalence of pulmonary TB and HIV among TB suspects in rural community in Southwest Ethiopia

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Background: The burden of TB and rate of TB-HIV co-infection in Ethiopia is not well documented because of the poorly developed diagnostic facilities, poor notification system and low health service coverage. The objective of this study was to measure the prevalence of pulmonary TB among TB suspects in a rural community in Ethiopia.

Methods: From February to April 2009, we conducted a community based survey in Gilgel Gibe Field Research Center, Southwest Ethiopia. TB suspects who had cough of 2 weeks or more were identified in all households and gave two sputum samples (morning-spot) and blood for the diagnosis of TB and HIV. Smear microscopy and culture was done to diagnose TB.

Results: A total of 29 257 adults in 10 882 households were screened for pulmonary TB. From the total population, 476 TB suspects were identified. About 32% of TB suspects had cough for more than 8 weeks. 220 (46.3%) had not yet sought help for their illness. We identified 5 and 17 new cases of pulmonary TB by smear microscopy and culture respectively. Four cases of pulmonary TB were on anti-TB treatment during the survey. From these figures, the prevalence of pulmonary TB was calculated as 71.8/100 000. All of the rural TB suspects were negative for HIV. From 89 urban TB suspects, 5 (5.6%) of them were positive for HIV.

Conclusion: The prevalence of culture confirmed pulmonary TB is low as compared to the WHO estimate. A substantial proportion of TB cases were not identified by smear microscopy. The numbers of undiagnosed cases of pulmonary TB that were identified through this survey are an indication of poor health care seeking behavior, resulting in a pool of infectious cases. Active case finding should be strengthened by the health extension workers and community DOTS program. Regional culture facilities should be strengthened to support the diagnosis of TB.

PC-100080-14   TB-HIV co-infection in California during the HAART era, 1996–2007

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Background: California reports the highest annual number of tuberculosis (TB) cases and over 12% of all persons living with HIV in the US. To assess trends at the intersection of these epidemics, we analyzed statewide surveillance data.

Methods: Incident cases reported to the California TB registry from 1996 to 2007 were cross-matched with the state HIV/AIDS registry. Incidence rates of TB with and without HIV co-infection were analyzed. Sociodemographic, clinical characteristics, and treatment outcomes were examined.

Results: 2392 (6%) of 39 718 TB cases during the study period were matched in the state AIDS registry. From 1996 to 2006, annual TB incidence among persons with HIV declined from 368/100 000 to 73/100 000, and without HIV declined from 12.7/100 000 to 7.3/100 000. Comparing the period 1996–2000 with 2001–2007, the proportion of TB-HIV cases increased among Hispanics (48% to 57%; $P < 0.001$), foreign born (46% to 63%; $P < 0.001$), and women (14% to 18%; $P = 0.06$), and decreased among Blacks (28% to 21%; $P < 0.001$). 77% of all foreign born patients with TB-HIV co-infection originated from Mexico or Central America; the median time from immigration to TB diagnosis was 10.7 (IQR 4–19) years. Median CD4 count at TB diagnosis was 78 (IQR 30–167). Patients with HIV co-infection were more likely to be sputum smear-positive (OR 1.17, 95%CI 1.08–1.28). Both isoniazid resistance (5% to 7%; $P = 0.07$) and pyrazinamide monoresistance (6% to 8%; $P = 0.01$) increased over time in TB-HIV cases but not in cases without HIV. In multivariate analysis, Hispanic ethnicity, older age, and injection drug use were negatively associated with treatment success among TB-HIV cases.

Conclusion: In California, the epidemiology of TB-HIV co-infection in the post-HAART era has shifted towards persons of foreign birth, women, and Hispanics. In addition, drug resistance has increased in TB/AIDS cases. These changes should be considered in focusing TB and HIV disease prevention and treatment efforts.

PC-100616-14   Tuberculosis in HIV positive individuals: our nine year experiences in Bydgoszcz, Poland

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The global impact of the converging dual epidemics of tuberculosis (TB) and human immunodeficiency virus (HIV) is one of the major public health challenges. The aim of the study was evaluate clinical presentions HIV-TB coinfection. We obtained retrospective review for cases of TB in patients with HIV infection treated in Bydgoszcz (Poland) from January 2001 to September 2009. During the study 49 cases (91.8% males, mean age 38.1; IVDU–70%) of TB in HIV infected adults were recognized. The mean CD4 cell count was 110.5 cells/mL (range: 0–650/mL), mean HIV RNA was $4.6 \times 10\,5$ (range >50–3.52×10^6) copies/mL. In 7 (14.3%) cases the diagnosis of TB and HIV were done at the same time. Clinical presentation included: 26–pulmonary TB, 11–disseminated TB, 12–extrapulmonary TB (3–meninigitis, 9–lymph nodes). In 4 cases TB was recogonized as immune reconstruction inflamatory syndrome (IRIS) with the onset of fever within 2–4 weeks after antiretroviral treatment (ART) initiation. The PPD skin test was negative for 2 of 5 patients with CD4 cell count $>$ 200 cells/mL and for 7 of 31 patients with CD4 cell count $<$ 100 cells/mL. Fever, night sweats, loss of weight and malaise were noted in all cases. The most common radiological findings in the chest X-ray were middle or lower lobe infiltrates, miliary infiltrates, hilar adenopathy. Normal X-ray was found in 21% patients with pulmonary TB. In all cases TB was confirmed microbiologiacally, but only in 2 cases acid fast bacilli were seen in sputum. 4.1% of patients were on ART for more than one year before TB, 86% commensed ART during TB treatment, which was associated with paradoxical worsening (TB-IRIS) in 2 (4.1%) cases. 12 patients with CD4 cell count $<$ 50 cells/mL at the time of TB diagnosis developed subsequent AIDS-defining diseases. We found a mortality rate of 16.3% (8 cases). In our region TB poses an increasing problem in population of HIV-positive individuals. HIV-TB remains a major challenge to global health.

PC-100261-14   Trends of TB-HIV co-infection in Nepal

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Aim: The HIV epidemic has increased the global tuberculosis burden. Addressing HIV associated tuber-

culosis is an important component of the new 'Stop TB Strategy' which builds on the DOTS strategy. Estimating the prevalence of HIV infection among TB cases can act as an early warning system for the spread of TB due to HIV and help in planning the programme activities accordingly. The aim of the study was to review the trend of TB-HIV situation in Nepal.

Methods: A Record Based Descriptive Study was carried out. The data were collected from the Annual Reports STAC and Annual Reports of National Tuberculosis Control Programme, Nepal which are published from 2003 to 2009.

Results: The prevalence of HIV in tuberculosis patients is rising in Nepal. First survey conducted in 1993/94 showed zero prevalence of HIV among TB patients. Surveys conducted in 1993/94, 1995/96, 1998/99, 1999/2000, and 2001/2002 showed 0.6%, 1.88%,1.39% and 2.44% prevalence of HIV among new TB patients respectively. Latest sentinel surveys of HIV among TB patients conducted in 2006–07 showed a prevalence of 2.4% and HIV prevalence among MDR-TB patients was 5.09%.

Conclusion: The prevalence of HIV is rising in Nepal. There is a need to conduct prevalence study at sentinel sites representing entire country and further study among MDR-TB patients. The TB and HIV/AIDS Control Programmes of Nepal need to urgently strengthen TB-HIV collaboration activities.

PC-100265-14   The 4th national HIV seroprevalence survey among TB patients in Cambodia: preliminary results

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Objective: Since 2003, Cambodia has been conducting national HIV seroprevalence survey among TB patients to monitor the trend of TB-HIV co-infection and to document the impact of TB-HIV collaborative interventions. The three national surveys conducted in 2003, 2005 and 2007 showed HIV prevalence among TB patients of 11.8%, 10% and 7.8%, respectively.

Methods: All new and re-treatment TB cases who were registered for treatment in the national TB programme in the month of July 2009 were eligible for the study. Transfer-in cases and patients who did not provide consent were excluded. This survey was an unlinked anonymous study. The serum which reacted to Determine HIV1/2 and Unigold HIV1/2 tests were considered as positive results.

Results: A total of 3130 TB patients were registered during the study period. Of these, we were able to contact and obtain blood samples from 2864 (91.5%)

TB patients. Overall HIV prevalence among TB patients was 6.4%. HIV prevalence among male and female was 6.5% and 6.0%, respectively. The highest prevalence of HIV was in the age group of 25–44 years old (14.8%). HIV prevalence of smear positive TB, smear negative TB and extra-pulmonary TB was 3.7%, 8.8% and 9.4%, respectively. When grouped by geographical areas, the HIV prevalence differed significantly from 0% in North-east provinces to 9.7% in Coastal provinces.

Conclusions: The prevalence of HIV among TB patients continues to decline in Cambodia. However, HIV prevalence among TB patients remains high. The declining trend reflects the trend of the HIV epidemic in the country (1.3% in 2003 to 0.9% in 2008) and possibly the impact of TB-HIV collaborative interventions that have expanded in recent years.

PC-100453-14   Incidence and risk factors for tuberculosis among HIV-infected patients in the HAART era

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Background: To access the factors associated with TB incidence among in HIV-infected patients in Taiwan.

Methods: Linked registered HIV and TB data in Taiwan CDC and national health insurance data from 1998 till 2008. Cox regression was used to estimate the incidence of tuberculosis. The observation duration was defined from the date of HIV diagnosis to the date of TB diagnosis, death or 31 December 2009. The incident TB case was defined as the TB diagnosis date at least 30 days after HIV diagnosis.

Results: Among the 16 601 HIV-infected persons, 753 cases were co-infected with TB. Excluded 80 cases had TB diagnosis before HIV diagnosis and 295 cases had concurrent HIV and TB diagnosis, 378 cases met the definition of incident TB cases after a median follow-up of 3.8 years. The TB incidence of HIV-infected persons was 0.6 persons per 100 person-years (PY), 95%CI 0.54–0.67 per 100 PY. TB incidence rate was higher in HAART-naïve patients than those ever HAART (HR = 1.70, 95%CI 1.36–2.13). Elevated risks of tuberculosis was also noted in older HIV-infected persons (HR = 1.02, 95%CI 1.01–1.03 for per year increase at HIV diagnosis). After adjust with HIV transmission categories, gender, education level, marriage status, the age at HIV diagnosis and HAART status, older age at HIV diagnosis and no HAART were still related to increased TB incidence. In HAART-naïve patients, patients who had HIV diagnosis over 40 years old had higher risk to develop TB (HR = 2.08, 95%CI 1.28–3.37). On the contrary, age at HIV diagnosis over 40 years or not show no difference in TB incidence rate among patients under HAART.

Conclusion: HAART was associated reduced TB incidence rates among HIV-infected persons. Old age was associated with increasing TB incidence, especially in patients without HAART. Additional strategies to further reduce the TB incidence are needed, such as preventive therapy for latent TB infection and enhanced adherence to HAART, especially in elderly patients.

PC-101337-14   Tuberculosis preventive therapy for HIV-infected persons in cART era: a cost-effectiveness analysis

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Background: Combination antiretroviral therapy (cART) reduces by 70–90% the risk of developing TB for persons with HIV and isoniazid preventive therapy (IPT) have a preventive effect additional to that of cART. Recently, new tools for diagnosis of LTBI (interferon gamma release assays—IGRAs) became available. Our aim was to analyze cost-effectiveness of IPT in persons with HIV in the cART era and to evaluate the impact of using IGRAs (T.SPOT-*TB* and QuantiFERON-TB [QFT]).
Methods: We estimated costs and outcomes for a hypothetical cohort of individuals newly diagnosed with HIV followed-up for 10 years using a Markov model. Unit costs were drawn from the reimbursement rates in the Italian National health system. Baseline characteristics of patients were based on a survey carried on in Italy. IPT was modelled as a reduction of probability to progress from TB infection to active disease. Use of cART impacted on probability of death and probability of developing TB. The main outcomes were defined in terms of costs per infection cleared and costs per case of active TB averted.
Results: Starting with a cohort of 4000 subjects (new cases of HIV infection in Italy in 2007) in our base case scenario, assuming a baseline prevalence of LTBI of 13%, 73.5% completed the screening procedure. Individuals with a positive test were 320 for TST, 226 for QFT and 507 for T.SPOT-*TB*. T.SPOT-*TB* minimizes screening costs per case of active TB averted (173 subjects needed to screen) but has the worst performance in terms of number needed to treat (16.1). The lowest costs per LTBI cured and per active TB averted resulted by using TST (995€ and 3670€ respectively).
Conclusions: Cases of active TB averted through screening and IPT are only a few in absolute terms (13–17 cases in base case scenario). TST is the diagnostic assay that showed the best cost-effectiveness ratio. Increasing the rate of completion of the screening process can significantly reduce cost-effectiveness (−15/−17% for TST).

PC-101310-14   HIV prevalence among TB patients compared with that of the general population in 14 states of Nigeria

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Background: TB and HIV/AIDS still remain major public health problems in Nigeria. The country ranked 4th among the 22 high TB burden countries globally and third in terms of HIV burden. The prevalence of HIV among TB patients increased from 2.1% in 1991 to 19.1% in 2001 (National HIV Sentinel survey) and it is now estimated to be 27%. The aim of this study is to find out if the HIV prevalence among registered TB patients in 14 states testing at least 75% of the TB patients for HIV is a reflection of HIV prevalence among general population.
Methods: A retrospective study of the records of HIV testing among registered TB patients compared with the result of the HIV sentinel survey conducted in each of the state in 2008. 14 States in Nigeria that tested at least 75% of their registered TB patients for HIV in 2008 were selected for this study.
Result: The prevalence of HIV among TB patients range from 27%–56% in states with HIV prevalence among the general population ranging from 7%–10%; the range is between 16.2% to 38.6% in states with HIV prevalence among the general population ranging from 5%–7%; the value is 16%–26% in states with HIV prevalence among the general population ranging from 2%–4% ; and 5.8% in state with HIV prevalence among the general population ranging from 1%–2%. The prevalence of HIV among TB patients is above 20% in states with HIV prevalence among general population of 4% and above and below 20% in those HIV prevalence among general population below 4%. Detail in the Table.

Table   HIV prevalence among general population and registered TB patients in 14 states in Nigeria that tested 75% of the registered TB patients for HIV in 2008

No.	States	HIV prevalence among general population in 2008 (%)	HIV prevalence among TB patients in 2008 (%)
1	Benue	10.6	37.1
2	Nassarawa	10	56.3
3	Akwa-Ibom	9.7	25.3
4	Cross River	8	34.7
5	Rivers	7.3	27.2
6	Enugu	5.8	30.9
7	Taraba	5.2	38.6
8	Lagos	5.1	24
9	Abia	5	16.2
10	Imo	4.6	18.5
11	Gombe	4	26.9
12	Ebonyi	2.8	16.5
13	Oyo	2.2	16.6
14	Osun	1.2	5.8

Conclusion: Most of the states with high HIV prevalence among registered TB patients also have higher prevalence of HIV among the general population; the prevalence of HIV among TB patients is therefore a reflection of HIV prevalence among general population. HIV will continue to fuel TB burden and therefore need for strengthen collaboration between NTBLCP and NASCP with special attention to areas with high prevalence of HIV.

PC-101436-14   HIV prevalence among tuberculosis patients in coastal districts of Gujarat, India

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Background: Lack of information about HIV prevalence among general population in coastal districts of Gujarat till 2006–07. Neither information regarding the burden of HIV among tuberculosis patients in Gujarat nor population based surveys have been previously reported. A community-based HIV prevalence survey was conducted among tuberculosis patients treated under the Revised National Tuberculosis Control Programme (RNTCP) to evaluate the HIV prevalence among tuberculosis patients in Coastal district of Gujarat.

Methodology: Two coastal districts (Junagadh & Porbandar) from 1600 km long sea coast line were stratified based on non availability of HIV prevalence in antenatal clinics and randomly selected. From December 2006 to April 2007, remnant serum was collected from patients' clinical specimens taken after 2 months of antituberculosis treatment and subjected to anonymous, unlinked HIV testing.

Results: Serum specimens were obtained and successfully tested for 409/569 (71%) tuberculosis patients eligible for the survey. HIV prevalence ranged widely among the 6 surveyed tuberculosis units (TUs) from 1.4% in Una TU to 7.2% in Vanthali TU. HIV prevalence among Tuberculosis patients was 3.4% in Junagadh district and 5.9% in Porbandar district. HIV infection was 4.4% among males and 3.1% among female tuberculosis patients. HIV infection was 1.9 times more likely among smear-negative patients and 4.5 times more likely among extrapulmonary patients relative to smear-positive tuberculosis patients.

Conclusion and recommendations: The burden of HIV among tuberculosis patients is found to be very high in coastal districts of Gujarat where no data on HIV prevalence among general population are available. HIV prevalence was higher among smear negative and extra pulmonary tuberculosis patients compare to sputum positive tuberculosis patients.

Intensified efforts from programme managers are required to implement comprehensive TB-HIV services.

PC-100940-14   Non-tuberculous mycobacterial in gold miners: evolving spectrum with increased HIV prevalence

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Background: Liquid culture is recommended for TB suspects in high HIV-prevalence settings. In the context of a trial of community wide isoniazid preventive therapy among gold miners (Thibela TB, South Africa), we describe characteristics of TB suspects from whom non-tuberculous mycobacteria (NTM) were isolated.

Methods: Sputum samples were collected from TB suspects at: 1: Screening for active TB at enrolment and follow-up for Thibela TB participants; 2: Routine mine primary care services. NTM species were identified using 16S rRNA sequencing. Clinical and laboratory records were reviewed and chest radiographs closest to date of sputum specimens read.

Results: Of 745 with positive mycobacterial cultures, NTM only were isolated from 232 individuals. 228/232 (98%) male, median age 44. Species isolated, smear status, HIV prevalence and radiograph interpretation ($n = 171$) shown in Table.

Species	Number isolated n (%)	Number smear positive[*]	HIV prevalence	Median CD4 [n]	CXR classified as definite/ probable TB
Detected at routine health services					
M. avium complex	25 (26)	2	8/10	87 [5]	2/14
M. kansasii	21 (22)	6	5/8	265.5 [6]	4/9
M. parascrofulaceum	9 (9)	1	3/3	102 [2]	1/7
M. fortuitum	9 (9)	2	1/1	[0]	1/5
M. gordonae	7 (7)	0	1/1	195 [1]	1/3
New species	7 (7)	1	3/3	355.5 [4]	0/5
Other species	18 (19)	0	4/5	291.5 [4]	1/7
Total	96 (100)	12	25/31	215.5 [22]	10/50
Detected by active screening					
M. gordonae	53 (39)	7	2/12	298 [9]	13/46
M. kansasii	29 (21)	11	9/14	198 [9]	13/25
M. avium complex	13 (10)	0	4/5	211 [4]	1/12
M. parascrofulaceum	12 (9)	2	1/2	223 [1]	4/11
M. fortuitum	11 (8)	0	3/5	358 [2]	5/10
M. szulgai	5 (4)	0	2/2	132.5 [2]	2/5
New species	3 (2)	0	0/0	[0]	1/2
Other species	10 (7)	0	3/3	311 [2]	1/10
Total	136 (100)	21	32/43	234 [28]	40/121

[*]Fluorescence microscopy.

Conclusions: NTM are common among TB suspects in this setting and a high HIV prevalence was found, approaching that of those with *M. tuberculosis*. *M. avium* complex has become more common compared with previous studies and may relate to high HIV prevalence. Knowledge of common species is important to guide effective treatment.

TB IN CHILDREN

PC-100948-14   Improving the in vitro diagnosis of TB in children? A study into the chemokine IP-10

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Background: In primary infection with *Mycobacterium tuberculosis*, the bacteria is incorporated and processed by antigen presenting cells. During this process cytokines and chemokines are released, which can be utilized in the in-vitro diagnosis of tuberculosis (TB). Interferon gamma (IFN-γ) is measured by an IFN-γ Release Assay (IGRA: QuantiFERON®-TB Gold In-Tube Test = QFT, T.SPOT®-*TB* = Elispot). Although these assays are highly specific, their sensitivity, especially in toddlers, is questioned. Recent data has shown that the chemokine IP-10 (IP-10) might be a promising biomarker for the in-vitro diagnosis of TB in children. We will be investigating whether IP-10 is as sensitive and specific as the more commonly used IGRAs at detecting mycobacterial diseases and infections in children with different ages.
Methods: We included 51 children ≤15 years (24 were <5 years) and divided them into 4 groups those with: 1) TB; 2) latent TB infection (LTBI); 3) non-tuberculosis mycobacteria infection; 4) controls. The IP-10 was measured by an ELISA after stimulation of the blood samples with ESAT 6 and CFP 10, highly specific TB antigens.
Results: The cut-off for IP-10 for both the TB group and control was set at 981.9 pg/ml. The levels of antigen-dependent IP-10 in TB and LTBI patients were significantly higher compared to the NTM and control participants. The correlation between antigen-dependent IP-10 and IFN-γ was significant in the TB and LTBI group ($r^2 = 0.576$, $P = 0.003$) and ($r^2 = 0.587$, $P = 0.001$). The antigen-dependent levels of IP-10 were 11.27 fold higher than IFN-γ.
Conclusion: The IP-10 measurement seems to be an alternative method to diagnose TB and LTBI in children and toddlers. The higher antigen-dependent IP-10 level may suggest a higher sensitivity especially in younger children with an immature immune system.

PC-100807-14   Resistant tuberculosis among Mozambican children

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Setting: The prevalence of resistant tuberculosis is increasing in the last decades. In Mozambique, the prevalence of resistant tuberculosis among adult population is 3.4%; in children, there is no data up to date. The objective of our study was to describe the profile of resistant tuberculosis among Mozambican children.
Methods: A transversal retrospective study was done between 2005 to 2009. Data were collected in the National Reference Tuberculosis Laboratoy (NRTL).
Inclusion criteria: All children under 15 years of age with positive cultures for BK were included in the study.
Results: A total of 80 children were selected; 54% of them were males and 46% were females with ages between 0 and 14 years. The more frequent age group was from 5 to 14 years. 54% of the total analysed specimens were sputum, 38% were gastric aspirate and 8% were not identified. 31% of the cases had proved microscopically negative for BK. Of all those specimens which were microscopically positive for BK, 74% were sputum and 53% were gastric aspirate. Concerning cultures for BK, only 26% of the cultures contained less than 20 colonies. A total of 34 cultures were tested for TB drug sensitivity. 18 cultures were found to be resistant; 31% were mono-resistant, 5% poly-resistant and 63% were multidrug-resistant.
Conclusion and recommendation: Mozambican children are infected early in life with resistant TB strains. Multidrug resistance was the main type of TB drug resistance among Mozambican children (63%). The principal resistance found was against isoniazid, rifampicin and streptomycin, the same founded among Mozambican adults (PNCT 2009). Contact tracing is recommended to be activated in order to identify and treat early affected children.

PC-100493-14   Hypothyroidism in children on ethionamide therapy

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Introduction: Ethionamide (ETH) is a frequently used second-line antituberculosis drug for childhood tuberculosis (TB). Limited adult literature suggests that hypothyroidism may occur on ETH therapy.
Aim: To determine the frequency of abnormal thyroid function tests in children on antituberculosis treatment including ETH.
Methods: We retrospectively assessed 137 children (mean age 4.9 years; range 0.3–15.8 years) hospitalized in Brooklyn Hospital for Chest Diseases, Cape Town for long-term anti-TB therapy between January

2008 and February 2010. All children on ETH and with a record of thyroid function tests were included. Elevated thyroid stimulation hormone (TSH) levels and decreased free thyroxine (fT4) levels were determined based on reference values provided by the suppliers of the analysers.

Results: High TSH and low fT4 (biochemical hypothyroidism) were documented in 41 (29.9%), high TSH with normal fT4 in 13 (9.5%) and isolated low fT4 in 28 (20.4%) children. The proportion of children with TB meningitis for each group was 12.2%, 23.1% and 3.6% respectively. Fifteen children received a treatment regimen including ETH plus para-aminosalicylic acid (PAS) of whom eight children (53%) had biochemical hypothyroidism. Of the children with an elevated TSH and a normal T4 only one had a goitre. Eighteen (13.1%) children received thyroxine supplementation. There were no differences in age, gender, HIV prevalence or type of TB in children with normal thyroid function and biochemical hypothyroidism.

Conclusion: Hypothyroidism seems to occur frequently in children treated for TB with a regimen including ETH. Children on ETH therapy should be monitored prospectively for hypothyroidism. A possible compounding effect of PAS should be further investigated.

PC-100770-14   Surveillance for tuberculosis in infants

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Background: The South African Tuberculosis Vaccine Initiative is involved in TB vaccine field studies.

Objective: To assess the yield of a surveillance systems to detect child TB suspects in a birth cohort study on TB incidence in children <2 years old.

Methods: Surveillance methods consisted of review of TB registers to identify cases and household contacts, hospital admission records and X-ray records, and home visits every 3 months for questionnaire based symptom screening. Suspects were admitted to a case verification ward for further TB diagnostics.

Results: Among the 4876 children who were enrolled in the cohort study, 928 were identified as TB suspects. 432 (47%) of these were detected during home visits, 255 (27%) were detected by hospital admission records review, 125 (13%) by TB registers review, 55 (6%) by referral from local clinics, 33 (4%) by review of X-ray records, 27 (3%) self reported directly to the study, and 1 unknown. TB was diag-

nosed in 364 (39%) of suspects. Amongst these, proportions detected by different methods were similar to the above proportions among suspects. Among the 92 (25%) TB cases that had been hospitalized shortly before admission to the research ward, 10 (11%) had been diagnosed with TB on discharge.

Conclusion: Home visits detected nearly half of suspects and cases. Hospitals admissions missed most TB cases. Although children were visited regularly at home, patient initiated contact with health facilities (hospitalization, clinic referrals, and X-ray) identified one third of cases, showing relevance of surveillance.

PC-100211-14   GAPS in care of paediatric TB-HIV in Mombasa District

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Setting: Mombasa district in Kenya.

Aim: TB clinics are entry points for HIV testing and subsequent referral to Anti Retrovial therapy. The objective of this study was to determine the prevalence of paediatric TB disease, HIV testing and care of the paediatric TB-HIV co infected patients in Mombasa.

Methods: A retrospective cross-sectional analysis was performed on routine program data for the period 1st January 2007 to 31st December 2007. District register supported by the facility register and patient record cards were utilized to extract the data.

Results: Of the 1402 patients registered in this period 156 were children (11%). 140 were pulmonary and 16 were extra pulmonary TB. The HIV testing rate for the paediatric TB patients was at 65% but only 12 children out of 46 (26%) among those less than 18 months were tested for HIV compared to 90 out of 110 (82%) for the children above 18 months. CPT uptake and ART uptake was at 94% and 12.5% respectively.

Conclusion and recommendation: HIV testing for children <18 months is low, there is need for introduction of viral test , (polymerase chain reaction) by dried blood spot in TB clinics. While Cotrimoxazole preventive therapy was good for those with confirmed HIV status at 94% the ART uptake even for those known to be HIV infected was low (12%). There is need for improved referrals between the TB-HIV clinics and the use of TB clinic as an entry point for paediatric ART scale-up.

PC-100756-14   Incremental value of ELISPOT assay for diagnosis of active tuberculosis in children

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Background: The diagnosis of tuberculosis (TB) in children is difficult. Interferon-gamma release assays (IGRAs) are promising tests for latent TB infection, but their incremental value beyond patient data and conventional tests for active disease has not been adequately evaluated. We applied multivariable analysis to smear-negative children with suspected TB in South Africa to determine the added value of an enzyme-linked immunospot (ELISPOT) assay in a high-burden setting.

Methods: Data were available for 171 children recruited from the Red Cross Children's Hospital in Cape Town, South Africa. Logistic regression models were used with culture result as the outcome. The initial model consisted of patient demographics and clinical signs. This model was extended, first by adding predictors for chest X-ray (CXR) and then the ELISPOT result. The area under the Receiver Operating Characteristic (ROC) curve was used to compare overall discrimination between models.

Results: From the initial multivariable model, age >24 months, weight-for-age Z score, history of contact, and cough >2 weeks were independent predictors of disease (the reduced model). The presence of lobar consolidation and lymphadenopathy on the CXR contributed significantly to the reduced model for estimating disease probability (ROC area 88.83% vs. 82.33%, $P = 0.04$). However, the ELISPOT assay did not show significant incremental value when added to the previous model with CXR results (ROC area 88.83% vs. 88.79%, $P = 0.98$).

Conclusion: In a high-burden setting, the ELISPOT assay does not appear to contribute significantly to estimating disease probability beyond patient data and conventional tests in smear-negative children. The use of multivariable analysis allows an informative approach to diagnostic research and has greater relevance for clinical practice. Further steps include the external validation of a scoring rule developed from the regression model to accurately predict or exclude TB.

PC-100927-14   Evaluation and outcomes of 'TB suspect' paediatric household contacts of adult MDR-/XDR-TB patients

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Background: The management of pediatric contacts of MDR/XDR-TB patients remains unclear and controversial. At our high TB and HIV prevalence site in rural KwaZulu Natal, household contact tracing is conducted for all new MDR/XDR-TB patients. Here we report on the preliminary evaluation and outcomes of TB suspect children living in the households of MDR/XDR-TB patients from 2005–08.

Methods: Beginning in 2005, all available children <12yo from MDR/XDR-TB patients' homes were evaluated. Parents/caretakers were interviewed regarding TB symptoms; children underwent tine test, chest X-ray (CXR), and doctors' assessment. HIV testing was offered from 2008. Selected children were treated with first line TB therapy based on clinical criteria and reevaluated 12–48 months after initial assessment.

Results: Of 74 TB treated children from 39 households, 25 (35%) were MDR-TB contacts and 49 (65%), XDR-TB contacts. Tine test ($n = 48$) was positive in 31 (65%) and CXR ($n = 51$) was abnormal in 38 (75%); all children with negative skin tests had abnormal CXR. Seven of 41 (17%) HIV tested were positive. As of February 2010, the first 48 (65%) have undergone reevaluation, a median of 22.6 months (IQR 20.3–24.9) after initial assessment. Twenty seven (60%) were healthy, one was diagnosed with XDR-TB; 2 died of unclear causes and 18 who were referred for sputum induction ($n = 12$) and blood culture ($n = 18$), based on clinical evaluation, were smear and TB culture negative after 8 weeks. One child with negative cultures and untreated HIV disease subsequently died.

Conclusion: This interim analysis shows that >90% of pediatric household contacts of MDR/XDR-TB patients who were themselves TB suspects and treated with first line TB therapy did not develop MDR/XDR-TB. This suggests they did not have transmitted disease from the index MDR/XDR-TB case. These data may help in the development of evidence based approaches to management of pediatric household contacts of MDR/XDR-TB patients.

PC-100506-14   Evaluation of the implementation of IPT amongst contacts of TB cases in a district in South India

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Background: Under the Government of India's Revised National Tuberculosis Control Programme (RNTCP), all household contacts aged <6 years of smear-positive pulmonary tuberculosis (PTB) cases are to be placed on isoniazid preventative therapy (IPT).
Objective: To assess the proportion of PTB contacts <6 years placed on IPT.
Setting: All smear positive PTB cases registered during April–June 2008 under RNTCP in Krishna district, Andhra Pradesh, South India.
Methods: Cross-sectional study. Data was collected through a semi-structured questionnaire after interviewing the PTB patient or household members. Demographics, personnel who provided IPT, reasons for not using IPT, ratio of PTB cases to <6 years contacts, were analyzed.
Results: Of 848 PTB patients registered, initial home visits by health staff were done in 569 (69%) of cases. There were 172 contacts <6 years of age, about 1 potential IPT eligible contact per 4.7 PTB cases. No case of active disease was found during screening of the contacts. Amongst these contacts, 97 (56%) were put on IPT; 57 (59%) were from urban areas and 40 (41%) from rural areas. 64% of all child contacts in rural areas and 10% in the urban areas did not receive IPT. Parent reported reasons associated with not receiving IPT included: no counseling about IPT (41%); no home visit by the health staffs (34%); and no isoniazid stock available at their health centres (25%).
Conclusion: Only 56% of eligible PTB child contacts were being placed on IPT as per RNTCP guidelines. Contacts in rural areas have 6.4 times more chances of missing out on IPT compared to urban counterparts. The integration and equitability of IPT delivery system in general health system is weak. The importance of IPT should be emphasized to health staff and field workers during their initial home visits.

TB TREATMENT INTERVENTION

PC-100696-14   Evaluation de la stratégie de circuit de lames tuberculose à Madagascar

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Introduction : A Madagascar, la stratégie de circuit de lames (CL) a commencé en 2005 avec le projet FIDELIS, durant 12 mois. A la fin du projet, 424 Centres de traitement (CT) ont été formés en CL. Après le projet, d'autres CT ont été ouverts soit par le PNT, soit par d'autres partenaires privés. Actuellement, il est nécessaire de connaître le nombre de centres ayant effectivement utilisé le CL, les résultats, les problèmes et difficultés rencontrés.
Objectifs : Déterminer si la stratégie a été efficace et efficiente pour le PNT et si la charge de travail accrue n'a pas eu d'effet négatif sur la qualité générale des laboratoires.
Méthodologie :
—Trois étapes pour l'étude :
—Questionnaires dans 30 centres de santé privés
—Questionnaires envoyés dans 92 laboratoires de Centres de Diagnostic et Traitement
—Observation directe sur terrain dans 49 CT ruraux, représentant 20% des CT et rattachés à 7 CDT
Résultats : 151 CT sur 260 (58%) formés en CL sont fonctionnels, 51 (22%) ont abandonné et 58 (22%) n'ont pas du tout fait. Les problèmes de ressources humaines sont les principales causes de non fonctionnalité des CT. L'acheminement des lames est assuré par les membres de la famille, dans 52% des cas. Les frottis de crachats ont été, en général de bonne qualité et bien lus aux CDT.
Conclusion : La stratégie CL a contribué à l'accessibilité du diagnostic dans les CT étudiés. Les résultats de contrôle de qualité des CDT ont été satisfaisants. Mais beaucoup reste à faire pour l'amélioration du CL, en particulier l'application des règles de biosécurité.

PC-101473-14   Apport du troisième crachat dans le diagnostic de la tuberculose pulmonaire

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Objectif : Evaluer l'apport du troisième échantillon d'expectoration dans le diagnostic de la tuberculose pulmonaire.
Patients et méthodes : Etude transversale portant sur 6707 patients colligés du 1er Décembre 2008 au 30 Novembre 2009 au Centre National Hospitalier de Pneumo-phtisiologie de Cotonou. Nous avons relevé,

à partir du registre du laboratoire, les résultats de la bacilloscopie des patients inclus. Les critères d'inclusion sont : être suspect de tuberculose pulmonaire et fournir trois échantillons ou plus d'expectorations, recueillis selon les recommandations de l'OMS. La coloration à l'auramine est celle utilisée. Nous avons déterminé la positivité de chaque échantillon, sa richesse bacillaire et le rendement supplémentaire des deuxième et troisième crachats.

Résultats : Sur les 6707 patients inclus, 1164 (17.4%) avaient eu une bacilloscopie positive sur l'un au moins des échantillons. Parmi eux, 1155 patients (99.2%) étaient positifs à la première série de trois échantillons et 9 (0.8%) dans la seconde. L'échantillon le plus fréquemment positif était le deuxième (1115), suivi du troisième (1061) et du premier (982). L'échantillon le plus riche en bacilles était le deuxième (809), suivi du premier (617) et du troisième (605). La bacilloscopie était positive dès le premier échantillon chez 982 sujets (84.4% des bacillifères). Le rendement supplémentaire du deuxième crachat était 158 patients (13.6%). Celui du troisième échantillon (15 patients soit 1.3%) comparé aux deux premiers était nettement plus faible (13.6% vs. 1.3%, $P < 0.0000$). Les deux premières crachats avaient détecté à eux seuls 1140 patients (97.9%).

Conclusion : Le troisième crachat apporte peu dans la détection des cas bacillifères. Le recueil de deux expectorations paraît suffisant pour le diagnostic. Une telle stratégie, avec ses gains économiques et temporels, semble intéressante dans nos pays aux ressources limitées.

PC-100177-14   Randomised control trials of 4 month rifampin and 6 month isoniazid for latent TB infection treatment

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Purpose: Treatment of latent tuberculosis infection (LTBI) with isoniazid (INH) is complicated by poor patient adherence and the need for close follow-up of side effects, especially hepatotoxicity in adults. Shorter and safer regimens are needed. The objective was to compare the rates of adverse events and treatment completion in 2 treatment regimens for LTBI treatment.

Materials and methods: A randomized, open-label trial for 6 months of isoniazid (INH) or 4 months of rifampin (RMP) was conducted in a prison in Northern Taiwan. Patients without a contraindication for INH and RMP and requiring treatment for LTBI treatment were enrolled. Adverse events resulting in drug discontinuation, and on-time treatment comple-

tion were compared. Hepatitis was defined as having blood levels of Glutamic Pyruvic Transaminase (GPT) ⩾3 times of upper limit of normal value (40 U/L).

Results: A total of 374 patients started LTBI treatment and 81.8% completed it. The completion rate was significantly lower for 6 months of INH compared to 4 months of RMP (77.2%, vs. 86.3%, RR = 0.89, 0.81~0.99, $P = 0.02$). Development of hepatitis was observed in 25 patients, solely in INH treatment arm, not in RMP arm ($P = 0.0000177$, Fisher's Exact test). In INH treatment arm, 25.5% of the hepatitis C carriers could not complete the treatment and the relative risk was 3.09 (3.09, 1.46–6.52, $P = 0.0023$) compared to non chronic hepatitis carriers (8.3%), which was not observed in B carriers.

Conclusion: LTBI treatment with 4 months of RMP led to fewer hepatitis and thus higher completion rate compared to 6 months of INH. Hepatitis C carriers need regular follow-up for liver function during INH treatment due to higher incidence of hepatitis.

PC-100403-14   An internal quality control system in clinical trials: does it make a difference?

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Background: Errors made by clinical research teams conducting clinical trials potentially impact on participant rights and quality of data. Internal Quality Control (QC) by the research team may reduce these errors.

Objective: To describe improvement in error detection rate for the Informed Consent Form (ICF) and source documentation using an extended QC system versus conventional peer-review QC.

Methods: In a tuberculosis vaccine trial, peer-review QC and an extended QC system were used. During peer-review a team member checks the work of a colleague in the field. For the extended QC system dedicated internal QC officers use customized electronic checklist tools to check the ICF and the participant source documents on which critical study data is recorded. ICF errors were categorized as major if the ICF was invalid according to good clinical practice (GCP) guidelines and minor if it was valid but needed corrections.

Results: Four-hundred-and-twenty (420) sets of ICF and source documents were checked. Ninety-seven (97; 23%) errors were identified by extended QC that had been missed by peer-review QC. Of these 48 (49%) were ICF errors—66% of them minor and 33% major. Forty-nine (51%) instances of blank or

inaccurate entries in source documentation fields were identified.

Conclusion: An extended QC system in a clinical trial using dedicated internal QC officers identified errors in the ICF and source documentation not identified by conventional peer-review.

PC-100644-14 Polymorphisms of uridine-diphosphoglucuronosyl transferase1 in anti-tuberculosis drug hepatitis

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Background: The three phases of detoxification are oxidation, conjugation, and transportation. The oxidation reaction is mainly catalyzed by cytochrome P 450 (CYP), while UDP-glucuronosyltransferase (UGT) is the major enzyme involved in the conjugation reaction, with a number of proteins responsible for the transportation of toxic metabolites. Of these three detoxification phases, oxidation has been the most studied, while conjugation and transportation are newer areas of research focus in the 21st century.
Design/method: This study investigate the relationships between detoxification protein gene polymorphisms and anti-tuberculosis drugs induced hepatitis (ATT hepatitis). 222 TB infected cases (80 cases and 142 controls) are included in analysis and some samples are exclude due to the incompetence of demography data.
Result: Genotypes of UGT 1A7*1/*3 may increase the risk and severity of anti-TB drug-induced hepatitis as the odds ratio (OR) are 2.52 (95%CI = 1.05–6.03), Genotypes of CYP2E1 C1 genetic may increase the risk and severity of anti-TB drug-induced hepatitis as the odds ratio (OR) are 1.87 (95%CI = 1.15–3.05) than C2 genotype. The synergistic effects were found between UGT1A7*3 and CYP2E1*c1 in the study. The Odds ratio of 13.20 (95%CI = 4.55–38.28) was found when patients with both UGT1A7*3 and CYP2E1*c1 genotype.
Conclusion: This study indicated that the UGT 1A7 polymorphism may correlate the ATT drug-related hepatitis among TB patients in Taiwan. Checking liver enzymes and detoxification genotype before treatment and regular monitoring liver enzymes during treatment are highly recommended. Application of pharmacogenetics or pharmacogenomics, such as assessing UGT genetic polymorphism, may help prevent this hepatotoxicity. The results from these investigations will prove to be helpful for understanding the ATT induced hepatitis and provide novel insights in controlling mycobacterial infection in our population.

PC-101455-14 Poor quality chest radiographs hinder accurate diagnosis of smear-negative pulmonary tuberculosis

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Background: Clinical algorithms to diagnose smear negative pulmonary TB require the performance of a chest X-ray (CXR). Current research aims to maximise the utility of diagnostic radiography using structured proformas such as the Chest radiograph Reading and Recording system (CRRS). Accurate interpretation relies on high quality film production. In resource constrained countries where radiological staff are few, clinicians anecdotally describe quality to be a major hindrance in the correct interpretation of CXRs.
Aim: To systematically assess the quality of CXR used in diagnosis of TB in a Malawian teaching hospital.
Methods: 50 randomly selected CXRs from TB suspects were reviewed by 5 clinicians of different grades (consultant radiologist, clinical lecturer, clinical officer registrar, medical intern and medical student). A structured proforma describing film quality was completed for each review.
Results: No films contained date of birth or details regarding projection. 73% had no clear name, 61% were of poor penetration, 58% had no date of examination, 58% were obscured by artefacts, 51% were rotated, 46% had absent side marker, 39% were not visually sharp, 33% were not of good inspiration and 19% did not show the entire lung field. Overall, readers rated their confidence in interpreting the film based on quality at 65% (95%CI 61–71). 13% (CI 8.6–17.4) of films were deemed unreadable, 80.5% (CI 79–91) less than ideal, and only 6.5% (CI 0–14)
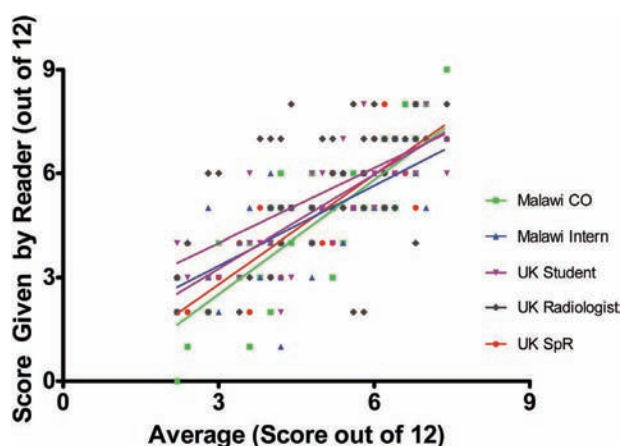
Figure Correlation between readers.

to have no technical problems hindering interpretation. Clinicians of different grades were in agreement on 80% of occasions.

Conclusion: All grades of clinician were agreed that interpretation of the majority of films is hindered by technical limitations. In parallel with investigating the utility of structured proformas for the interpretation of CXRs, educational, motivational and infrastructural effort is required to enable the performance of adequate quality films in low resource settings.

PC-100784-14   Default from treatment among urban tuberculosis patients, Kampala, Uganda

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Background: Retaining patients on their tuberculosis treatment is a challenge in urban settings. We assessed defaulting and the risk factors associated with defaulting in Kampala, Uganda.

Methods: We conducted an observational study among adult, TB treatment-naive patients receiving treatment at three urban primary care clinics in Kampala where treatment supervision is community-based. Programmatic defaulting was defined according to the Uganda National Tuberculosis Program as having missed two monthly clinic visits by a patient not reported to the clinic to have died or continued treatment elsewhere. Defaulters were actively followed up and those found interviewed. We defined true defaulting as having missed two monthly clinic visits by a patient known to be alive and not continuing treatment elsewhere. Factors associated with programmatic defaulting were analyzed by multivariable logistic regression.

Results: Between April 2007 and December 2009, 270 adult TB patients were included. The median age was 30 years (range 16–83), 160 (59%) were male, and 236 (87%) had treatment supporters. Fifty-four patients (20%) defaulted, of whom 26 (48%) were not found despite several home visits. Of the 28 patients followed up, 2 (7%) had died, 8 (29%) had continued treatment elsewhere and 18 (64%) had stopped treatment. Thus, the overall true defaulter rate was between 7% (18/270) and 16% (44/270). Female patients were less likely to default compared to male patients (adjusted OR 0.3; 95%CI 0.1–0.8, $P = 0.007$), as were patients with female treatment supporters compared to those with male supporters (adjOR 0.5; 95%CI 0.2–1.0, $P = 0.046$). Age, educational level, employment, marital status, distance of

residence from the health center and having HIV infection were not associated with defaulting.

Conclusions: Defaulter rates in this setting are high. Treatment support in urban populations requires more attention, in particular the potentially favorable role of women.

TB EDUCATION/ADVOCACY/ SOCIAL ISSUES

PC-100378-14   Training patients on TB and HIV at TB services in Central Asia

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Background: According to National TB services of the Central Asian Region (CAR), 40–60% of TB patients in Kyrgyzstan, Kazakhstan and Tajikistan do not complete the course of treatment and 30% practice HIV risk behaviors. With a TB epidemic in which 25% of cases are MDR-TB, this may cause the danger of HIV-TB and HIV/MDR-TB co-infection spread.

Intervention: To prevent infection by increase adherence to treatment and decrease the patients behavior risks AFEW provides CAR's National TB-services with technical support aimed at establishing a thematic standard trainings with patients, including Training Module, and 'Patient School' monitoring. Twelve seminars were conducted for 260 penitentiary and public health nurses. The legal base for nurses' activity in TB services and for their training program at educational agencies was also improved.

Results and lessons learned: The 'Patient School' practice is regulated by appropriate orders from the Ministries of Health in each country. More than 1500 patients have been trained by nurses. Once trained, patients train their peers. Adherence to treatment has grown from 63% to 96%. The number of persons who wish to undergo HIV tests has also increased, as well as visits to drop-in centers where patients can get sterile syringes, condoms, and information materials, and to Social Bureaus, where they can get medical and social services.

Conclusions: Patient training increases the efficiency of treatment by 30%. At the 'Patient School' patients obtain knowledge, behavioral skills and emotional support in order to decrease the risks of disease transmission, including MDR-TB and HIV-TB.

PC-100487-14   Development of a generic training manual for tuberculosis prevalence surveys

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Background: Twenty-one countries have been advised by the World Health Organization (WHO) to conduct a tuberculosis (TB) prevalence survey before 2015. Streamlined processes of data collection are essential in these surveys. Training ensures that there are standardised procedures throughout the survey. Several countries had requested for guidance on training modules therefore, we developed a generic training manual.

Response: The content of the training manual was based on experiences from prevalence surveys conducted in several countries and based on protocols for surveys to be implemented in the future. The target population for the training manual is prevalence survey staff at central and field team level.

Results: Besides one general introduction module, different modules were developed for the teams at central and field level. Each module contains an overview of the objectives, materials, responsibilities, methodology, timing, duration and background materials. Practical exercises and assessment of trainees are part of the module. The four modules for the central level team are: laboratory procedures, chest X-ray procedures, survey management and monitoring and data management. The modules for the field level teams include modules for ethics and procedures in household surveys, census taking, interviewing techniques and practicing in dummy households. Additionally, training modules on specific technical procedures were developed for the chest X-ray team and laboratory team. For the team leaders a module on survey management and data checking was developed.

Conclusions: It is expected that in 2010 several countries will start using this training module to ensure standardized training of all staff involved in TB prevalence surveys. The training manual will become available in public web domain after the experiences of these countries have been incorporated to ensure the value of the manual for other countries planning a TB prevalence survey.

PC-100635-14   Quality of DOTS training courses in Afghanistan

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Background: In Afghanistan, NTP has prioritized to develop an enormous health workforce for quality TB control program. However, quality of trainings has not yet been evaluated. Thus, this survey aimed to evaluate the quality of the various training courses conducted by NTP to develop necessary interventions to enhance effects of trainings.

Method: A cross-sectional descriptive study was conducted. Quality of 11 training courses was evaluated by direct observation of NTP central staff. Quality of 20 facilitators was evaluated by trainees in regards with 5 degrees (excellent, good, fair, acceptable and not acceptable).

Result: In all training programs pre and post test were taken but in only 7 occasions scoring was taken soon after the test. Only in 54% of training courses training modules authorized by NTP were used. 70% of facilitators had taken training of trainer course (TOT) besides initial DOTS training course. Those trainers with TOT had better training skills than those without TOT in various points. Especially, in emphasizing on main point, eye contact, giving examples, knowledge on subject, material use, and use of methodology, there were significant differences between trainers with TOT and those without TOT, see the Table for more detail.

Table   Evaluation of trainers' training skill

Trainers skill	Excellent (%)		Good (%)		Fair (%)		Acceptable (%)		Not acceptable (%)	
	TOT	No TOT	TOT	No TOT	TOT	No TOT	TOT	No TOT	TOT	No TOT
Encouraging for participation	92.3	85.7	7.7	14.3	0	0	0	0	0	0
Use of methodology	77	42	23	58	0	0	0	0	0	0
Considering trainees level of knowledge	84.6	71.4	15.4	28.6	0	0	0	0	0	0
Clarity of explanation	61.5	57.1	38.5	42.9	0	0	0	0	0	0
Emphasize on main points	92.3	42.9	7.7	42.9	0	14.2	0	0	0	0
Briefing of session	61.5	57.1	38.5	42.9	0	0	0	0	0	0
Question response	76.9	71.4	23.1	28.6	0	0	0	0	0	0
Eye contact	92.3	57.1	7.7	42.9	0	0	0	0	0	0
Feedback	84.6	85.7	15.4	14.3	0	0	0	0	0	0
Class control	84.6	71.4	15.4	28.6	0	0	0	0	0	0
Voice projection	84.6	85.7	15.4	14.3	0	0	0	0	0	0
Relevancy of examples	100	42.9	0	57.1	0	0	0	0	0	0
Trainer knowledge	84.6	57.1	15.4	42.9	0	0	0	0	0	0
Material usage	84.6	43	15.4	57	0	0	0	0	0	0

Conclusion: Overall the quality of DOTS training courses and trainers were good, but usage of training modules should be improved. The results indicated the importance of TOT for quality of trainers and

NTP should develop plans to develop qualified trainers by TOT.

PC-100798-14   TB KAP study in Tajikistan: results from the general population

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Background: In 2005, a survey was conducted throughout the country among patients, healthcare providers and the general population to determine their knowledge, attitudes and practices about tuberculosis (TB). Advocacy, communication and social mobilization activities were designed and implemented based on the results, and the survey was repeated in 2009. The objective of this study was to assess differences in TB-related knowledge and attitudes in the general population from 2005 to 2009.
Methods: 1037 members of the general population from 10 pilot areas in all five regions of Tajikistan were administered structured interviews. Respondents were randomly sampled from local Jamoat population registers.
Results: Analyses from general population data showed that there were improvements in several areas compared to 2005. The proportion with no knowledge of any TB symptoms fell from 25.3% to 7%, and of those citing cough increased from 63.7% to 84.9%. Of respondents, 83.9% thought TB could be cured (70.8% in 2005). The proportion of respondents without any knowledge of means of TB transmission fell from 10% to 5.2%. Population attitudes contributing to discrimination changed slightly, with those recommending isolation of TB patients rising from 84% to 94.4%, while reasons for not accepting a former TB patient into the family included fear of infection (48.9%), that TB is inherited (25.2%; 2005: 26.6%) and risk of re-infection (24.1%; 2005: 19.7%).
Conclusion: Population knowledge on many factors increased, yet results illustrate that attitudes reflecting discrimination towards TB patients persist. Inaccurate perceptions of TB transmission, the basis for discriminatory behaviors, continue, despite country-wide educational and informational campaigns. Further campaigns should continue and intensify dissemination of accurate TB transmission information.

PC-100387-14   Across the wire: using radio to ignite public discussion on TB and HIV in Zambia

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Aim: Recognizing the need for increased health-awareness among the public and in an effort to harness the power of the media to influence public debate and change behaviour, the Zambia AIDS-Related Tuberculosis (ZAMBART) Project developed a 12-part radio programme series focused on the symbiotic relationship between TB and HIV.
Methods: The series, which ran from February 22–May 17, 2010 on ZNBC Radio Two, featured a different ZAMBART researcher each week discussing topics such as the TB-HIV relationship, Zambia-South Africa TB and AIDS Reduction (ZAMSTAR) Study's community interventions, TB stigma, the changing role of home-based care, the Three 'I's and TB and food security. With an average listener base of more than 1.7 million people and spanning the entire country, the radio series attracted listener participation from as far north as Solwezi and as far east as Chipata (on the border with Malawi).
Results: One of the more enlightening aspects of this radio series was the misconceptions that listeners held on TB and HIV (based on the caller contributions and questions) and as such highlighted the fact that more radio programme series are needed to reach the mass population with accurate health promotion messages. To help bridge this gap, ZAMBART will edit and standardize the contents of the radio series to produce a complete volume of TB-HIV programmes and then package it for broadcast on community radio stations throughout the country, starting first with the ZAMSTAR study intervention areas. Using the 'ripple in the pond approach', ZAMBART is seeking to maximize the voice of the organization and the impact of its initial TB-HIV radio programme series to reach an even more diverse audience.
Conclusion: The majority of Zambians remain unaware of the intricate relationship between the two diseases; therefore, the responsibility falls to researchers, NGOs and journalists to improve the current public health environment in the country.

PC-100897-14   Evaluation of TB peer educators: essential partners in metropolitan TB control

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Background: One in six of all notified tuberculosis (TB) cases in London are among homeless people, problem drug and alcohol users and prisoners (hard-to-reach). These groups are at high risk of delayed

diagnosis, infectious and drug resistant TB and poor treatment outcomes. The Berlin Declaration (2007) stated that affected communities are essential partners in TB control. While initiatives involving hard-to-reach communities in HIV control have proven effective, evidence to support their contribution to TB control activities is lacking. We aimed to improve service access and uptake of screening among hard-to-reach groups by harnessing the authentic voice and experience of former TB patients from these affected communities.

Method: Seven former TB patients with experience of homelessness and drug/alcohol dependence were recruited and trained as peer educators to work alongside TB clinics and a mobile screening service. Qualitative and quantitative methods were used to evaluate their impact on service access and screening uptake.

Results: Peers recruited 3200 hard-to-reach clients at 101 screening sessions resulting in 45 hospital referrals between May 2009 and February 2010. Following training for homeless hostel workers from TB peers, screening uptake increased from 44% to 75%. Structured interviews with service users highlighted the importance of peer educators in raising TB awareness and promoting service access.

Conclusion: Our evaluation demonstrated that trained peer educators can improve service access and screening uptake and provide an authentic voice of experience that homeless people can relate to. Peer involvement should be integral to tackling metropolitan TB among hard-to-reach groups.

PC-101414-14   The role of communication in the management of TB in Kenya

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Background: One of the greatest challenges faced in the management of TB in Kenya, is stigma, which affects the health seeking behavior and the adherence to treatment. To address these issues surveys were conducted and intense public education campaigns carried out in the country.

Intervention: Information was gathered through a KAP survey at the workplaces, rapid surveys carried out in public places and forums, one-on-one interviews with specific target group and online surveys. The results of these surveys led to the development of the LIVE LIFE TB FREE campaign (signs and symptoms), TB INA TIBA campaign (treatment and cure) and TALK.LEARN.LIVE campaign (prevention, patient rights and responsibilities).

Results: 96.2% of the respondents cited the media campaigns and printed material as the source of information. TV&Radio Infomercials, transit advertising, posters, brochures, facts sheets, Point-of-sale advertising, magnet theater, web clips and documentaries were some of the channels used. Disease prevention and improved health seeking behavior are strengthened by appropriate information and knowledge in the population. Persons who know the modes of TB transmission, associated risk factor, and possible signs and symptoms are more likely to take appropriate action in earnest.

Conclusion: Provision of the right TB information empowers the public to take appropriate action for their protection and seek early and adhere to treatment as necessary. Communication indeed plays a major role in TB management and it needs to evolve with the times.

PC-101432-14   The knowledge of the Brazilian population on tuberculosis

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Background: Brazil has the 18th highest number of tuberculosis (TB) cases in the world. It is an important public health problem, with 80 000 new cases per year. The PFG-TB Brazil supports the Brazilian government in controlling the disease. To guide public policy is important to investigate the population's knowledge about the disease, i.e. causes, symptoms, treatment, stigma and prevention. The lack of baseline studies on the national question motivated the present study.

Methods: A quantitative household survey-type was implemented through 3340 interviews with semi-structured questionnaire applied to residents living in 53 municipalities randomly sampled. The research was targeted at multiple stages stratified by municipality, sex, age and educational level.

Results: Demographic characteristics: 50.1% are male, 87.2% have up to 59 years. The socio-economic characteristics: 56.7% have incomes up to US$792.00; 70.5% are homeowners and 69.4% live in homes where up to 4 people cohabit. In relation to TB, 51.0% claim to have knowledge about the disease; 81.3% said that TB is a communicable disease and 47.8% that it is transmitted by cough. About transmission, 51.0% of the responses can be considered as containing stigmas. Of those that know the symptoms, 87.1% reported cough 34% of the subjects reported knowing someone who had or has the disease.

Conclusion and recommendations: The research will help to define actions for tuberculosis control in Brazil, whereas the information about the disease and its determinants is essential to increase the cure, treatment adherence and reducing stigma.

PC-101406-14   Motivation and de-motivation study amongst health care workers in Kenya

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Background: Human resource is central to TB control in the country and determines access to service and quality of care. Health worker care retention is a major challenge. Addressing health worker motivation and de-motivation is key. The study identifies factors affecting health worker motivation in public and private TB care settings. It also looks at use of Human Resource management tools.

Method: Cross sectional study on health care workers. This entailed administration of structured questionnaires and focused group discussions. A total of 359 health workers across the cadres participated from randomly selected district and sub-district hospitals, health centers and private facilities. The data was entered in EPI INFO and analyzed using STATA.

Results: The study factors affecting motivation are encouragement and rewards (70.47%) and the desire to adhere to professional goals and values (56.55%). The main de-motivators are lack of supplies and equipments (62.12%) and high workload (53.48%). The use of Human Resource management tools was satisfactory with 67% of health workers having received on job training, 66% had undergone performance appraisal and more than two thirds rating it as good. 95% of the respondents felt that supervision was supportive.

Conclusion: Personal goals are important to health care worker; however an enabling environment is requisite. This includes correct use of human resource management tools and providing supplies and equipments. Non-financial incentives are important motivators to staff motivation and these include encouragement and rewards, acknowledging their professionalism and addressing their professional goals such as recognition, career development and other qualifications.

TOBACCO CONTROL/PROGRAMMES/ LAWS AND POLICIES

PC-100013-14   Status of the smoking cessation and its costs in Eastern Mediterranean countries in 2009

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Background: Among the basic responsibilities of health care institutes in various countries is treatment of tobacco dependence. Methods applied have different costs and do not affect all people the same. Treatment is influenced by local environment and culture as well as individual interest and needs. This study was designed with the purpose to address the situation with smoking cessation efforts and its expenditure and to provide basis for future studies and implementing tobacco control programs across countries in the region.

Methods: This was a cross-sectional observational study prepared succeeding the third Intergovernmental negotiation body in regards to illicit tobacco trade protocol of the framework convention on tobacco control in July 2009 in Geneva, Switzerland. The study was in form of questioning participating country representatives from the Eastern Mediterranean region who were all either focal point individual or expert in tobacco control programs. Information needed included methods for tobacco cessation, cost of services including counseling by primary physician or specialist, gum or nicotine patch, Zyban, champix and other practices were collected.

Results: In 11 countries (52.4%), smoking cessation programs and counseling was directed by primary physicians. Also, 9 countries (42.9%) provided services through specialists. In 13 countries (61.9%), nicotine gum and in 14 countries (66.7%) nicotine patch is accessible in pharmacies. In 6 countries (28.6%), Zyban (Bupropion 150 mg) and in 7 countries (33.3%), Champix (Varnicline 1 mg) are available at pharmacists with written prescription. The mean costs of each service were higher than a pack of cigarette significantly.

Conclusion: In countries with support services for tobacco cessation, directors need to provide care at society level, less costly and accessible for everybody and in countries where such programs have not been initiated, it is recommended that effort to do so occur.

PC-100014-14   Evaluation of the smokers' knowledge and attitudes about implementation of pictorial health warning

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Background: Given the approval and completion of the Comprehensive National Tobacco Control Law's executive guidelines in 2007 we decided to study on the smokers' knowledge and attitude about this issue before and after the implementation of this law (fall 2008 & spring 2009) and we were going to find the pictures influenced on the smokers.

Material and Methods: It was a cross-sectional study which was done in two stages on the sample size smokers in different districts of Tehran. In the second stage of the study, exactly the same people were ques-

tioned again. The indicators including 'cigarette smoking, knowledge about the mentioned law, the picture quality and selection, and its effect on smoking pattern' were questioned and observed.

Findings: In the first stage 1731 smokers and in the second stage 1590 smokers were questioned. In the both stages, male smokers were about 70%. In the first stage knowledge about the law was about 40%, while it was 95% in the second stage. The adequate effect of the law in the first stage was 33% and it was 7% in the second stage. The picture quality was good reported 10% and it ranked the last one (1.7%) among all the selected pictures. The picture of buerger disease was at the top of the choices 43.4%.

Conclusion: The attitude toward this law's efficacy has not been changed. The anticipation of smoking reduction after the law implementation has not been proven.

PC-100015-14   Is smoke-free legislation enforced completely in Tehran in 2009?

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Introduction: Creating smoke-free public places is essential to protecting non-smokers and also motivates smokers to quit. Recent smoking ban in public places in Iran and its weak enforcement, led to decision to study the circumstances in Tehran.

Materials and Methods: This was a cross-sectional study which has been done during the year 2009. First, Tehran's geographic map was divided into 3 areas north, center and south and subsequently, 10 sub locations in each area were selected randomly. From the sub locations, easy sampling was done going straight in the right direction to collect enough cases. The evaluated indicators included 'the existence of smoking ban signs, ashtrays and smoking areas and also the way of showing objection to smoking.'

Results: Four hundred fifty eight restaurants and food courts were studied. In 60 places (13%) there were no smoking bans sign. In 140 places (30%) there were ashtrays and in 54 places (12%) there were smoking areas. In 132 places (29%), owners had no objection against smoking. All cases were aware of smoking ban in public places. More than 50% considered it a useful law and 106 restaurants (23%) believed that the law would increase number of customers. There was no statistical relationship between the location and years of business with abiding the law, but significant correlation between smoking ban signs with owner objection against smoking and increased number of customers was found ($P = 0.000$).

Conclusion: In spite of long time adaptation to the law, it has not been fully implemented and reinforced.

PC-100545-14   Semen quality of male smokers and non-smokers in infertile couple

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Introduction: Smoking adversely affects spermatogenesis and sperm fertilization potential. Our objective was to assess effect of smoking on sperm analysis and its parameters.

Material and method: In a cross-sectional study, 180 men of couples with at least 1 year primary infertility attending Avicenna infertility clinic were evaluated for medical tobacco consumption status and semen analyze.

Result: 180 men (71 smoker and 109 non-smokers) were studied. Cigarette smoking was negatively correlated with sperm concentration. ($P = 0.01$) but there was not any significant correlation with sperm count, morphology and motility. Further more, cigarette experience follows the same pattern of correlation as cigarette smoking.

Conclusion: Although the effect of smoking on infertility remains inconclusive, smoking consumption and even its experience had an adverse effect on sperm concentration.

PC-100844-14   The first Quit-Line in the region: experience from Iran

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Background: After many years establishing the first smoking cassation clinic in Iran we know that due to some difficulty many smokers can not to attend quit program and they would like to have some consultation via telephone call. In this study we evaluated the efficacy of Quit-line for the first time in smoking cessation.

Methods: 2 general practitioners were trained for consulting in quit line. The quit program was consisting of 4 sessions with 1 week interval. Our telephone counseling was both reactive and proactive in 8 AM till 5 PM during 2005–2008. In reactive counseling, the smoker initiates, all calls and talks with counselor about specific issues of current concern. In proactive counseling, the counselor calls the smoker and provides counseling in a systematic manner, with scheduled sessions similar to traditional cessation clinics. Smoking status was based on self-report and regular follow-up was conducted after quit day and some of

them were selected randomly for confirming abstinent by CO Respiratory test.

Results: 1000 cases made contact. 520 of them give some brief information and answer about smoking and treatment. 480 cases of all subjects entered in cessation programs. 80% of them were male. The mean age was 38.5–7.9 years. 72.7% of participants were married. 75.2% of subjects were educated. 51.3% of cases had high nicotine dependency. 332 cases had brief advice to quit and 148 people continued to complete their course. 122 cases (82.4%) quit after at least 4 sessions. The abstinent rate after 1, 3, 6 and 12 months was respectively 59%, 41%, 31 and 18%.

Conclusions: This method is an appropriate and accessible method which can be used in smoking cessation counseling.

PC-100874-14   The Union Grants Program—progress in granting under the Bloomberg Initiative from 2007 to 2010

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The Union has been a partner in the Bloomberg Initiative to Reduce Tobacco Use (BI) Grants Program for over 3 years. Over that time The Union has developed and contracted more than 90 grants across over 20 countries. This presentation will examine the statistics of grants across WHO regions (Africa, Middle East, Europe, Latin America, South-East Asia and Asia Pacific) including organization types, funding areas, funding amounts and grants focus. The presentation will also split the information into the top 5 countries with the highest number of smokers in the world, the next 10 priority countries and the rest of the world, showing the numbers of grants funded against the percentage of smokers. The presentation will also explain the types of grants offered by The Union and the evoluation of grants processes under the BI.

PC-101303-14   Tobacco control in Bangladesh: present situation and future directions

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Background: Bangladesh ratified FCTC in 2004 and enacted tobacco control (TC) law 2005. Since then Ministries and NGOs have been working together to implement and enforcement of TC law. One of the important elements of TC law is functioning of taskforces (coordinating body) at different levels. Taskforces monitor the progress of TC law implementa-

tion and enforce law through mobile courts where violations are found.

Interventions: TC law implementation was intensified in Bangladesh since 2007 with the support of Bloomberg Initiative to Reduce Tobacco Use. About 40 district and 100 sub-district taskforces have been activated till 2009. In later part of 2009, all Bloomberg Initiative in-country partners, grantees and Ministry of Health and Family Welfare reviewed the progress of TC law implementation and made recommendations for actions.

Lessons learnt: It was found that mobile court is one of the unique instruments in enforcing TC law for expanding of smoke-free activities and intensify ban of tobacco advertisement, promotion and sponsorship (TAPS). Print media publicized news on 22 mobile courts widely in 2009. The mobile courts also raided Dhaka Tobacco central store and BAT head office to investigate any irregularities.

Conclusion: Strengthen TC law enforcement using mobile courts by taskforces is essential. For effective use of taskforces, amendment of the TC law to address identified weaknesses to comply with FCTC is prerequisite to control tobacco in Bangladesh.

PC-100398-14   Smoke-free policies are popular and supported in Egypt. What next?

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Egypt has the highest cigarette consumption in the Middle East and North Africa region (MENA). The Egyptian parliament has promulgated Laws on tobacco control that prohibits smoking in all its forms in all indoor public and workplaces. At present the proper enforcement of the law has been a challenge primarily due to lack of enforcement structure and protocols to assist enforcement authorities. The Union Middle East Office in collaboration with the CAPMAS and the MOH-Egypt have conducted a survey among 427 (206 males and 221 females) randomly selected adults (aged 15 years and above) covering the major 7 districts of Alexandria governorate. The main purpose of the survey was to assess public opinion in regards to 100% smoke-free legislation and its implementation by Alexandria City Government. Face to face interviews were conducted using pre-tested structured Arabic questionnaire. High agreements regarding the harmful effects of smoking and exposure to SHS were professed by all respondents. Alexandria residents (smokers and non smokers) unanimously supported the right of customers and employees to breathe clean, smoke-free air in workplaces & public places over the right of smokers to smoke inside public places & workplaces. Our results also revealed

that almost all interviewed residents in Alexandria (98%) expressed their strong support to the Alexandria City Government in enacting 100% SF indoor legislation in public places, work places and public transportation. No difference was identified regarding the support of SF policies enactment between never smokers and ever smokers (97.6% versus 99.3% respectively, $P > 0.05$). Furthermore 98.6% of the Alexandrians endorsed the plan of the City Government to implement the legislation ensuring 100% SF public and workplaces. The results of the poll clearly supports results concluded by different countries worldwide that smoke-free policies are popular and supported by the public.

PC-101040-14   How to improve lung health by preventing or limiting tobacco industry interference in public health

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Aim: The lung health of whole populations could be improved if governments and lung health groups used FCTC Article 5.3 Guidelines to prevent or limit tobacco industry interference in public health legislation and tobacco control policies. By systematically monitoring and countered tobacco industry tactics, civil society can help to remove barriers by monitoring, exposing and countering tobacco industry tactics that are blocking legislation and policies to improve lung health.

Methods: An inventory of all known TI tactics and marketing ploys was compiled from published articles, industry reports and informants, and key steps identified to:

- monitor and record the scope of TI tactics used to interfere in health policies;
- identify misleading industry claims;
- implement counter strategies; and
- evaluate changes and impact of implementing counter strategies.

Results: A guide for monitoring, exposing and countering TI interference in health policies was developed and tested in the 'dark market' of Australia. The guide identified key steps for:

- Establishing a monitoring system for all known types of TAPS and tactics
- Exposing and challenging TI tactics using graphic and current examples
- Countering TI claims and myths aimed at weakening legislation and policies
- Challenging lack of transparency and accountability over TI tactics that damage lung health
- Winning political support for adoption of FCTC Article 5.3 Guidelines as a minimum.

Conclusion: A systematic and comprehensive approach to monitoring and countering TI interference

can reduce interference and improve the level of political and public support for more effective public health legislation.

EPIDEMIOLOGY: TB IN LOW-BURDEN COUNTRIES

PC-101284-14   Tuberculosis al sur del Brasil: características de enfermos que procuraron servicios de salud, 2009

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Objetivo: Describir las características de los enfermos de tuberculosis que procuraron los servicios de salud en Pelotas/Brasil.

Métodos: Estudio descriptivo, de abordaje cuantitativo, realizado a partir de cuestionario estructurado aplicado a 102 personas residentes en el municipio de Pelotas (RS), que hicieron tratamiento para tuberculosis en el año de 2009.

Resultados: De las 102 personas que buscaron el servicio de salud en la presencia de los síntomas de la enfermedad 74,5% eran de género masculino, 55,9% se declararon como blancos y 34,3% negros. El estado civil de los sujetos en mayor proporción es soltero (51,0%), 42,2% se identifican como católicos, a pesar 27,5% se consideró sin religión. En relación a la escolaridad, 77,5% presentarón de 0 a 8 años de estudio, 31,4% están desempleados, siendo la misma proporción (31,4%) de empleados y 21,6% jubilados. El ingreso mensual mediano de las famílias de los entrevistados fue R\$600.00 (range R\$0.00–R\$5000.00/ R\$1.81 = US\$1.00), siendo R\$280.40 el ingreso medio mensual por persona de esas familias. A respecto del local de vivienda, 99,0% tienen casa propia, localizada principalmente en área urbana (97,1%). Sobre los hábitos y costumbres, se verificó que 37,25% de los sujetos usaron siempre o casi siempre las bebidas alcohólicas, 32,35% a veces y 30.39% casi nunca y nunca, 68,62% usarón siempre o casi siempre el cigarro y 22,55% nunca.

Conclusión: Resultados del estudio muestran que los hombres son mas afectados por la tuberculosis, siendo en su mayoría blancos viviendo en área urbana, con bajo nivel de escolaridad y renta familiar. Se identifica el consumo significativo de alcohol y cigarro que son importantes factores de riesgo para la demora del diagnóstico y abandono del tratamiento. Las características de los enfermos debe ser una constante en la evaluación, planeamiento y monitoramiento de acciones de salud y en la atención al enfermo.

PC-101292-14   Community-based case finding of TB-HIV patients in Kampala, Uganda

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Background: Case detection of TB and/or TB-HIV is central to successful control of the dual epidemics. Standard approaches for case detection have been employed by National TB programs as recommended by the World Health Organization. Innovative community-based approaches may contribute to early detection, timely linkage to care and improved outcomes such as survival.
Objective: To assess the effectiveness of community-based screening for TB and TB-HIV co-infection and linkage to care.
Design and methods: A cross-sectional house-to-house survey was conducted in Rubaga division of Kampala from January 2008–June 2009. Subjects aged 15 years or older consented to participate. Measurements included a questionnaire to identify chronic coughers (cough > 2 weeks), TB-related symptoms, rapid HIV testing, and tuberculin skin tests (TST). Two smear examinations were done and rapid HIV testing was performed based on the Uganda Ministry of Health recommendations.
Results: Of the 5103 participants, 199 (4%) reported chronic cough. We identified 39 (20%, 95%CI 14%–25%) new cases of active TB. Among chronic coughers, 85 (43%, 95%CI 36%–50%) were HIV positive, 53/85 (62%) were new HIV diagnoses. Of 22/199 (11%) TB-HIV+ co-infected persons, 11 (61%) were not in care. All newly identified TB, TB-HIV and HIV infected cases were linked to appropriate care.
Conclusions: Community based case-finding was effective in identifying undiagnosed TB, TB-HIV and new HIV cases in Kampala. Among chronic coughers, one in five had smears positive TB, about two in five had HIV infection and about one in ten were TB-HIV co-infected. These findings highlight the potential utility of community-based approaches in increasing case detection in high-burden settings.

PC-101478-14   Association between the seasonality of TB incidence, sunlight and Vitamin D concentration

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Background: Tuberculosis (TB) incidence has been reported to increase in summer months in several countries and the reasons are unclear. Skin exposure to sunlight increases Vitamin D (VitD) blood-levels, which may augment anti-TB immunity. We therefore studied the chronological association of TB diagnoses, the onsent of TB symptoms, VitD blood-levels and sunlight.
Methods: The study was nested within a micronutrient supplementation trial in a shantytown in Northern Lima, Peru. Average monthly TB incidence was calculated based on the number of cases diagnosed. The date of symptom onset was determined at interview. 292 measurements of VitD blood-levels were done from 2003–2005 and below-median VitD concentration was classified as low. Average daily sun hours data were obtained from historical records.
Results: Any effect of oral VitD supplementation on blood-levels was overwhelmed by a major effect of season. Winter months with fewer sunlit hours resulted in more people with low VitD concentration. Consequently the trough in VitD blood-level in winter was 23% lower than the peak in summer (56 vs. 43 nmol/l) and the average concentration was significantly different between these two seasons ($P = 0.0005$). TB symptoms rose along with an increasing fraction of the population having low VitD-levels and peaked 1–2 months after low VitD-concentrations became most prevalent. TB diagnoses peaked a further two months later in the beginning of summer in Peru (median delay between symptom onset and diagnosis: 60 days, interquartile range 30–95).
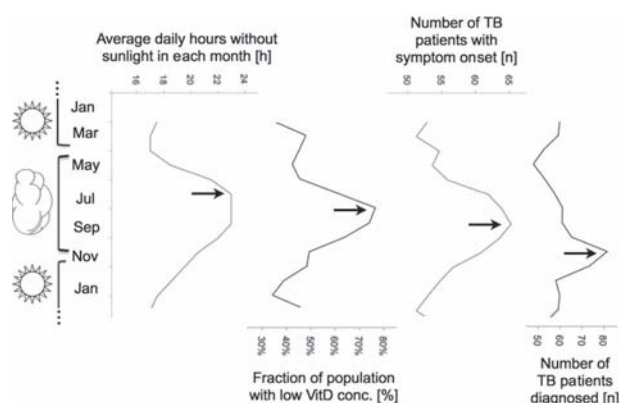
Conclusions: These observations suggest an explanation for the enigmatic summer peak in TB cases. The winter fall in sunlight caused a fall in Vitamin D levels that may impede antimycobacterial immunity. Assuming a 2-month TB incubation period, this potentially explains the subsequent increase in TB symptoms followed by a summer peak in TB diagnoses.

PC-101482-14   Are re-treatment TB cases at increased risk of treatment default? Insights from TB program data

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Setting: Two urban communities in Cape Town, Western Cape Province, South Africa with annual tuberculosis (TB) notification rates exceeding 1000 per 100 000 (all cases). Rates of TB re-infection after successful treatment were shown to be higher in these communities than rates of new TB.
Objectives: To investigate whether a history of previous TB treatment is associated with increased risk of treatment default; to assess the reliability of register data on re-treatment status.
Methods: Retrospective study using 2002–2007 routine register data from 2 TB clinics. The reliability of re-treatment status recorded under 'patient category' was estimated using treatment outcome information of a previous episode obtained via probabilistic record linkage as a reference. Treatment defaulters (cases) were compared to patients who completed their regimen (controls), using multivariable logistic regression.
Results: The sensitivity of re-treatment category was 90.8% for re-treatment after success and 78.1% for previous default. Of 141 treatment defaulters, 78 (55.3%) had a history of previous treatment. Multivariable analysis suggested re-treatment after treatment success (OR 1.77; 95%CI 1.13–2.78; $P = 0.01$), after default (OR: 6.37; 95%CI 3.69–10.99; $P < 0.001$) and after failure (OR: 13.28; 95%CI 3.90–45.25; $P < 0.001$) were each independently associated with present 'treatment default', along with 'male sex' ($P = 0.008$), 'age 19–39 years' ($P = 0.02$), 'positive sputum-smear' ($P = 0.02$), and 'summer season' (Dec–Feb; $P = 0.03$).
Conclusions: 'Patient category' used in TB registers as a standard variable for treatment history might be subject to considerable misclassification as records rely on self-reported history. Re-treatment cases seem at increased risk of treatment default, even after previous successful treatment. More research is needed to understand the causes of treatment default. Treatment adherence should be ensured especially in the context of high recurrence rates.

PC-100005-14   Birth cohort effect on latent tuberculosis infection prevalence, United States

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Background: Latent tuberculosis infection (LTBI) prevalence in the United States decreased approximately 60% in the three decades between 1971–1972 and 1999–2000 National Health and Nutrition Examination Survey (NHANES) surveys. We examined the effects of birth cohort on LTBI prevalence over time.
Methods: Our outcome was LTBI prevalence based on TST positivity, defined as an induration of 10 mm or greater in reaction to purified protein derivative S-1. Using weighted data analysis to account for sample survey design, we calculated the difference in LTBI prevalence between 1971–1972 and 1999–2000 for birth cohorts corresponding to 5-year intervals (1912–1916, 1917–1921, 1922–1926, 1927–1931, 1932–1936, 1937–1941, 1942–1946). We used sample variances derived from weighted data to calculate 95% confidence intervals (CI) around prevalence estimates and around prevalence differences. Prevalence differences comparing 1999–2000 with 1971–1972 estimates were considered statistically significant if the 95%CI excluded 0.

Table   Latent tuberculosis infection prevalence by birth cohort and sample year, United States

Birth cohort	Latent tuberculosis infection prevalence 1971–1972	Latent tuberculosis infection prevalence 1999–2000
1942–1946	5.05%	8.34%
1937–1941	7.30%	5.28%
1932–1936	8.97%	4.70%
1927–1931	16.78%	8.51%
1922–1926	19.47%	7.06%*
1917–1921	22.29%	2.71%*
1912–1916	16.05%	3.60%*

* Significantly different from 1971–1972.

Results: LTBI prevalence was significantly lower in 1999–2000 compared to 1971–1972 for cohorts born in 1926 or earlier (19% versus 5%), but not for cohorts born 1927–1946 (9% versus 7%). Adjustment for cohort restriction and foreign-birth did not qualitatively change the results.
Conclusions: Although older age groups have higher rates of TB infection than younger groups, nationally representative U.S. data suggest that observed LTBI prevalence in older people represents an underestimate of infection, because of the birth cohort effect and waning immunologic reactivity.

PC-101212-14   Exogenous reinfection as a cause of recurrent tuberculosis in an intermediate-burden country

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Background: Rate of exogenous reinfection in recurrent tuberculosis is variable in each country. We conducted RFLP analysis using IS*6110* in some pulmonary tuberculosis patients treated from public health centers since 2003.

Objective: To clarify the contribution of exogenous reinfection in recurrent tuberculosis in an intermediate-burden country.

Methods: We recruited patients experiencing two or more episodes of tuberculosis between the year 2003 and 2008. The results of genotyping pattern and susceptibility testing were compared between the two episodes. Treatment outcomes of initial episode were also analysed.

Results: A total of 41 patients who had been experienced two or more episodes of tuberculosis were recruited. The mean age at the initial episode was 36 ± 15 years old. The isolates from five patients in their two episodes showed different RFLP patterns. Three (12.5%) among 24 treatment success cases, one (9.1%) among 13 defaulted cases, one of two transfer-out cases showed different RFLP pattern. All the three treatment failure cases revealed the same pattern. One recurrent patient with the same RFLP pattern showed acquired drug resistance from pan-susceptible to MDR at the second episode. There was no difference ($P = 0.1754$ by Wilcoxon Rank Sum test, two-side test) in recurrent interval after completion of initial episodes between the two groups of identical (666 ± 488 days) and different (924 ± 376 days) RFLP patterns.

Conclusion: Exogenous reinfection has limited contribution to the recurrent tuberculosis in an intermediate-burden country.

PC-100301-14   TB in Australian-born in Queensland: still a gap between the Indigenous and the non-Indigenous

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Background: Queensland, Australia's second largest state, has a low tuberculosis (TB) incidence rate with most cases of TB found in immigrants. We studied the characteristics of the Australian-born TB cases in 2002–2009 to compare the Indigenous and the non-Indigenous population.

Methods: Retrospective review of the information recorded in the Queensland Tuberculosis Control Centre database of all TB cases in Australian-born persons notified between January 1st 2002, and 31st December 2009. 2006 Census data from the Australian Bureau of Statistics were used to calculate incidence rates.

Results: In the 8-year period 2002–2009, 1046 cases of TB were notified in Queensland. Seventy-nine cases (7.6%) were in patients from Aboriginal and/or Torres Strait Islander origin (ATSI), who form 3.3% of the total population in Queensland. One hundred and forty-four cases (13.8%) were in non-Indigenous Australian-born patients (NIAB). The crude incidence rate for ATSI in this period was 7.7 per 100 000 population, 13 times that of NIAB in the same period. The age-adjusted ATSI incidence rate was more than 20 times that of NIAB in all age groups above 25 years (Figure). Among patients with pulmonary TB, 63% of ATSI were sputum smear positive, compared with 45% of NIAB. Among ATSI patients there were no HIV positive cases, while among NIAB there were five (3%). Positive outcomes of treatment (cured or completed treatment) were recorded in 83% of ATSI and 87% of NIAB.
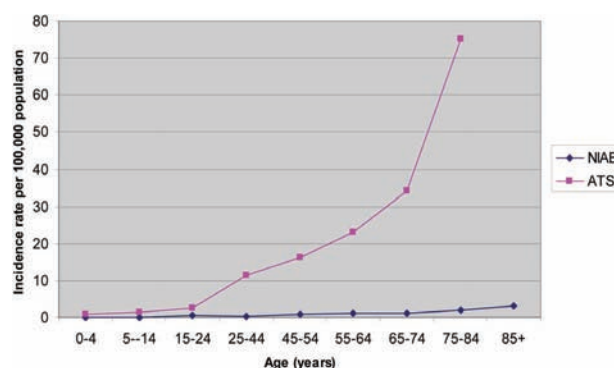
Figure TB incidence rate per age group in Australian-born patients in Queensland, 2002–2009.

Conclusions and recommendations: Although actual numbers of TB cases among the Australian-born population in Queensland are low, incidence rates for the ATSI are still much higher than for the NIAB and there is more advanced disease. This requires further exploration of access to health services and community involvement in TB education. We also need to look at sources of ongoing transmission in the Indigenous community and to identify the best means of applying preventive treatment.

PC-100703-14   Latent tuberculosis infection among health-care workers in the country of Georgia

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Background: Nosocomial transmission of tuberculosis (TB) is a major challenge of TB control in Georgia especially with emergence of multi and extensively drug-resistant (M/XDR) TB. A cross-sectional study was conducted between March–August 2009 to assess the prevalence and risk factors for LTBI using the tuberculin skin test (TST) and the QuantiFERON-TB Gold in Tube (QFT-IT) test and acceptance of having routine testing and treatment for LTBI among Georgian HCWs involved in TB control.

Methods: HCWs completed a questionnaire, had 3 ml of blood drawn for the QFT-IT test, and had a TST read 48–72 hours after placement.

Results: A total of 126 HCWs were enrolled; mean age was 38 years, 100 (79%) were women reflecting the gender distribution of HCWs in Georgia, 69 (55%) had a daily exposure to patients with TB. Overall, 74 (59%) had a positive result for at least one of the LTBI diagnostic tests; 71 (56%) had a positive TST and 46 (37%) had a positive QFT-IT; 43 (34%) were positive for both tests and 52 (41%) were negative for both tests. There was a moderate agreement between the two tests (75%, k = 0.524 95%CI [0.390, 0.659]); 28 (22%) had a positive TST but a negative QFT-IT and 3 (2%) had a positive QFT-IT and negative TST. 121 (96%) believed that routine testing for LTBI among HCWs is necessary and only 51 (40%) considered LTBI treatment appropriate for a HCW with a positive diagnostic test for LTBI. In multivariate analysis, a positive QFT-IT was associated with daily exposure to TB patients (OR = 3.14, 95%CI [1.19, 8.30]), and independent predictors of positive TST were daily exposure to TB patients (OR = 5.52, 95%CI [1.53–19.86]), and age $\geq$35 years (OR = 5.59, 95%CI [1.77–17.67]).

Conclusion: A high prevalence of LTBI was noted among Georgian HCWs; daily contact with TB patients and age $\geq$35 years was associated with an increased risk of LTBI. Acceptance of LTBI treatment among HCWs was low, possibly due to a high prevalence of M/XDR-TB in the country.

PC-100845-14   Risk factors associated with a tuberculosis outbreak in a northern Canadian population, 2007

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Background: Incidence of tuberculosis (TB) in First Nations and Inuit people remains above the national average and non-Aboriginal populations, with an annual case rate of 23.4 per 100 000 in 2006. Multiple factors contribute to a higher incidence of TB in Canada's North, including delay in diagnosis, limited access to healthcare, and crowded housing conditions. In 2007, a TB outbreak was declared in a Canadian Northern Community leading to a doubling of the annual territorial case rate.

Objective: To determine risk factors contributing to the outbreak.

Methods: Retrospective chart review of the index case, secondary cases and all high-risk contacts. Demographics and data related to contact tracing were extracted from the Northwest Territories Public Health outbreak database. Information on social risk factors and duration of contact with the index case at a local shelter (13 beds per room) was recorded.

Results: The index case was diagnosed with sputum smear positive pulmonary TB following six months of symptoms. 14 active pulmonary TB cases were identified through contact tracing. Outbreak strain was confirmed by PFGE in 13 cases. 112 high-risk contacts were identified of which 26 were randomly selected and matched as controls. Cases did not differ from controls in alcohol use, homelessness, co-morbidities, history of incarceration or ethnicity (Aboriginal). Cases shared the same shelter room with the index case more often than controls (29 vs. 4 days, respectively, P = 0.002) over the six month period.

Conclusion: Overcrowding and delay in diagnosis remain an important factor in the transmission of TB in populations at risk in Northern communities. Improved access to health care and measures addressing crowded living conditions in this high risk group are needed.

MDR-TB MANAGEMENT/TREATMENT

PC-100160-14   Impact of aminoglycosides on time to sputum culture conversion in multidrug-resistant tuberculosis

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Objective: The best dosage of aminoglycosides in treatment of multidrug-resistant tuberculosis (MDR-TB) is still unknown. We conduct this study to assess the impact of aminoglycoside dose on time to sputum culture conversion in MDR-TB patients.
Design: Retrospective observational cohort study.
Patients: 89 consecutive patients with pulmonary MDR-TB treated with the DOTS-Plus strategy between May 2007 and November 2009.
Measurements: Time to sputum culture conversion.
Results: Among 89 patients, 76 (85%) converted and 13 (15%) did not within one year follow-up. Compared to the patients with sputum conversion, patients without sputum conversion tended to have lower accumulation dosage of aminoglycoside within first 2 months of treatments (345 ± 113 vs. 542 ± 55, $P = 0.168$, respectively). Using Cox proportional hazards model, patients without previous treatment for tuberculosis (HR, 3.78; 95%CI 1.27–11.21, $P = 0.017$), no cavitation on chest radiograhy (HR, 1.91; 95%CI 1.20–3.04, $P = 0.007$), aminoglycosides accumulation dosage > 300 mg/kg within first 2 months (HR, 1.54; 95%CI 1.19–1.99, $P = 0.001$) and accumulation dosage > 600 mg/kg within first 6 months (HR, 1.63; 95%CI 1.03–2.59, $P = 0.037$) were associated with shorter time to sputum culture conversion. Multivariate analysis identified aminoglycoside accumulation dosage > 300mg/kg within first 2 months (HR, 2.08; 95%CI 1.23–3.52, $P = 0.01$) as an independent predictor of more rapid sputum conversion.
Conclusions: MDR-TB patients having aminoglycoside accumulation dosage > 300mg/kg within first 2 months was significantly associated with a more rapid rise in sputum conversion.

PC-100284-14   Prevalence of poor treatment adherence and its risk factors among MDR-TB patients in Manila

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Aim: To describe the degree of and risk factors for irregular MDR-TB treatment.
Methods: Retrospective review of clinical charts of

MDR-TB patients enrolled for treatment in 3 MDR-TB clinics of Manila, Philippines from 7/2003 to 10/2005.
Results: 240 of 261 enrolled MDR-TB patients had complete records and were included in the study. None of them was HIV-seropositive. Over the whole treatment period, 10.4% (25/240) had poor adherence (>20% of treatment days missed); 70% (168/240) had average adherence (>2% but less than 20% of treatment days missed); and 19.6% (47/240) had good adherence (<2% of treatment days missed). Treatment adherence deteriorated over time: The proportion of patients with poor adherence increased from 3.8% during the first 2 months of treatment to 13.9% in the continuation phase ($P < 0.001$) (Figure). In the past, 53% of the patients used
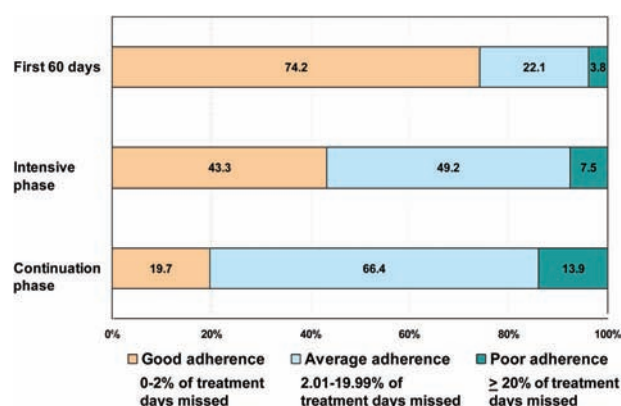
Figure   Degree of treatment adherence among 240 MDR-TB patients during the first 60 days of treatment, the total intensive phase and the total continuation phase.

to consume alcohol regularly. Among them, good adherence was less common than among the patients without former alcohol consumption (12% vs. 29%; $P = 0.002$). In the multivariate analysis, patients with poor adherence were compared with patients with good adherence; only former alcohol abuse suggested an increased risk for poor adherence ($P = 0.054$). Of the 210 patients who reached the continuation phase, 36% (76/210) were decentralized from the MDR-TB clinics to local DOTS centers. 19.7% of these 76 patients had poor adherence, compared to 10.4% (14/134) of those staying at an MDR-TB clinic ($P = 0.07$). No association was found between adverse drug reactions and poor treatment adherence.
Conclusion: Irregular treatment is common and increases during treatment. Patients decentralized to local DOTS centers tend to have poorer treatment adherence than patients treated at MDR-TB clinics. Interventions aimed at increasing adherence, e.g., psychological support, especially for those with a history of alcohol consumption, are warranted. Providers need special skills to motivate patients to take treatment regularly.

PC-100347-14   MDR-TB treatment in Kenya: cohort description from the first program

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Background: The MDR-TB prevalence in Kenya is estimated at 1.9% of new TB cases. In 2006, MSF started the first DR-TB program in the country in two sites. This is a description of the cohort of patients included and the preliminary results of the program.

Methods: Retrospective and descriptive study of the patients included in the program from May 2006 to February 2010. Patient's files have been reviewed. Epiinfo 6 used for the data analysis.

Results: Out of the 50 patients started on MDR-TB treatment, 24 (48%) were male and 48 adults. The average age of the adults was 32 years (19–57). Half of the patients, 54% were clinically stable at the first consultation. The average weight in adults was 52.4 kg (32–82) and 33% had a BMI less than 17. Treatment regimens were individualized. Forty-four (88%) patients suffered at least one side effect: 29 (58%) gastritis, 22 (44%) nausea, 21 (42%) electrolyte disturbance, 16 (32%) hypothyroidism, 14 (28%) peripheral neuropathy, 7 (14%) psychosis, 6 (12%) joint pain, 5 (10%) depression, 5 (10%) acne, 4 (8%) raised creatitine, 3 (6%) hearing loss, 1 (2%) tinnitus, and 1 (2%) seizures. The first smear was positive in 81% (39/48) of the patients and the first culture in 81% (39/48). The average culture conversion rate was at 3.1 months (2–12). Nineteen (38%) patients were HIV+. Eleven (58%) were unstable at the first consultation and 6 (38%) had a BMI less than 17. At the end of February 10, 29 (58%) were still on treatment, 13 (26%) were cured, 5 (10%) died, 2 (4%) defaulted and 1 (2%) completed treatment. Among those started on treatment in 2006–7, the outcomes were worse in the group of HIV positive patients: 50% (4/8) cured versus 77% (10/13), 38% (3/8) dead versus 15% (2/13), and 13% (1/8) defaulted versus 8% (1/13). However, the differences were not statistically significant ($P > 0.05$).

Conclusion: MDR-TB program results are encouraging in a population with a high proportion of HIV+ patients.

PC-100736-14   Risk factors for treatment default among MDR-TB patients enrolled in the PETTS study in Latvia

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Background: Preserving Effective Tuberculosis Treatment Study (PETTS) is a prospective, observational cohort study designed to answer questions related to acquired resistance to second-line drugs (SLD) during MDR-TB treatment in 9 countries (Estonia, Latvia, Peru, Philippines, Russia, S. Africa, S. Korea, Taiwan, Thailand).

Objectives: The overall objectives of PETTS are to determine the rate of, risk factors for, and consequences of acquired resistance to SLD in MDR-TB patients. This analysis focuses on risk factors for treatment default in Latvia.

Methods: In 2005–08, 106 consecutive consenting adults with pulmonary MDR-TB starting SLD treatment were enrolled in Latvia. All patients underwent direct observation treatment throughout the course of MDR-TB therapy. Standard WHO definitions were used to compare defaults with favorable outcomes (cure/treatment completion).

Results: Of 106 patients, 20 (19%) defaulted and 67 (63%) had favorable outcome. Default was associated with history of imprisonment (47% vs. 17%, $P = 0.01$). Default was associated with associated with the number of previous episodes of TB. Patients who had 2 or more prior episodes of TB (6/18, 33%) defaulted more often than patients who had exactly 1 prior episode (5/47, 11%, $P < 0.05$). However patients with no prior TB (9/22, 41%) also defaulted more often than those with 1 prior episode ($P = 0.01$). Age, sex, martial status, employment, education, homelessness, alcohol abuse, co-morbidities prior to enrollment and adverse effects during MDR-TB treatment were not significantly associated with treatment defaults.

Discussion: We hypothesize that patients with 1 prior episode tried hard to adhere to treatment. Patents with 2 or more prior episodes may be habitual defaulters, while patients being treated for the 1st time have not yet fully understood the consequences of defaulting.

PC-100787-14   Preliminary report—Taiwan Multiple Drug Resistance Tuberculosis Consortium (TMTC)

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Purpose: In contrary to the conventional model of hospital-treated and government-DOT for MDR-TB patient care, Taiwan CDC launched a hospital-initiated, patient-centered treatment program (Taiwan MDR-TB consortium, TMTC) since May 2007. The aim of this study is to compare the process indicators between MDR-TB patients receiving TMTC care within 6 months of diagnosis of MDR-TB (TMTC group) and those not receiving TMTC care within 6 months of diagnosis of MDR-TB (control group).

Materials and methods: MDR-TB cases in TMTC that were diagnosed before Aug, 2008 with bacteriology evidence after Jan, 2007 were enrolled. The differences of sputum culture conversion rates were compared between TMTC group and control group by Cochran-Mantel-Haenszel (CMH) method with SAS 9.1 version.

Results: A total of 370 patients received TMTC care during the period were analyzed and 225 (60.8%) were classified as TMTC group. No difference was observed in gender, age, chronic disease and alcohol consumption habit between two groups, except patient classifications ($P < 0.0001$). The crude conversion rates were better in TMTC group than control group and the sputum culture conversion rate at 18 months was up to 87.6% in TMTC group (Figure). After stratification by patient classifications, the sputum culture conversion rate at 6, 12 and 18 months were still significantly higher in TMTC group. The probability of culture conversion at 18 months was 64% increment compared to control group (CMH Relative risk = 1.64, 1.38–1.95, $P < 0.0001$).
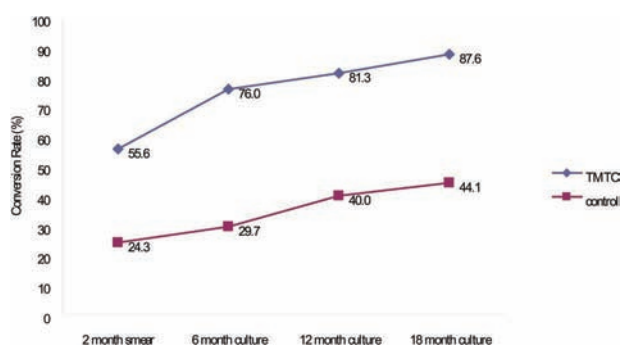
Figure   Crude conversion rates of sputum smear at 2 months, sputum culture at 6 months, 12 months and 18 months between TMTC group and control group.

Conclusions: The model of government-organized, hospital-initiated and patient-centered treatment, revealed better process indicators in this preliminary report. Further analysis for treatment outcome in long term follow-up is warranted.

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PC-100979-14   XDR-TB treatment outcome

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Introduction: Population-based studies on drug susceptibility of TB isolates recently conducted in various countries showed 4%–19% XDR-TB of all MDR-TB cases. Reported treatment outcomes among patients with XDR-TB vary considerably.

Aim: The aim of our study was to assess XDR-TB treatment outcome among patients managed at the Centre for Pulmonology and Tuberculosis (Minsk).

Method: 59 XDR-TB patients managed at the Centre in the period ranging from January 2004 to April 2010 with definite outcome were enrolled into the study. In all patients chemotherapy regimen was individually designed on the basis of drug susceptibility testing to both first and second line drugs.

Results: Out of 59 XDR-TB patients enrolled, 30 completed the treatment as planned (giving treatment success rate 51%), 12 (20%) patients died during the treatment, 10 (17%) patients had never achieved sputum conversion despite strict adherence to the treatment protocol, 7 (12%) patients abandoned the treatment and never restarted it again. Out of 59 patients 7 (12%) interrupted the treatment with following returning to treatment protocol, four of them completed the treatment, three died, two patient had never achieved sputum conversion. Out of 30 who completed the treatment, 25 declared cured giving cure rate 42%.

Conclusions: High mortality and low cure rate suggest employing new strategies to improve XDR-TB treatment outcome.

PC-100817-14   A retrospective analysis of possible renal toxicity associated with aminiglycoside in MDR-TB patients

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Aim: Aminoglycosides are one of the antibiotics that are often applied to treat the mycobacteria diseases. The main constraints the use of aminoglycosides are risks of nephrotoxicity and ototoxicity. Therefore, the aim of this investigation was to determine factors related to aminoglycoside-associated nephrotoxicity in MDR-TB treatment.

Methods: The clinical data of patients that contained sex, age, weight, height, history of accompanying chronic disease, serum creatinine, uric acid level, body weight adjusted aminoglycoside dose (mg/kg), the total accumulated dose of aminiglycoside before the nephrotoxicity come about and body surface area-adjusted estimated glomerular filtration rate (eGFR) were obtained and calculated from medical records and MDRD2 equation for further analysis. The patients with ESRD (End Stage of Renal Disaese) were excluded. The nephrotoxicity was defined as a 25% decrease in eGFR from baseline. The inference statistics, including Pearson χ^2 test, one-sample K-S test, unpaired t-test and multiple-linear regression.

Results: There were seventy patients with clinical and bacteriological proved MDR-TB cases enrolled. During the course of aminoglycoside therapy in the treatment of MDR-TB, nephrotoxicity were diagnosed in seventeen patients (24.3%). Patients who developed nephrotoxicity were significantly and inversely correlated with baseline eGFR ($P < 0.05$). Additionally, the female gender had higher incidence of aminiglycosides-associated nephrotoxicity than male (43.8% vs. 18.5%; $P < 0.05$). Although the potential nephrotoxicity associated with long-term use of aminoglycoside had been emphasized in the literatures. Fortunately, it was mild and reversible in most of our patients (94.1%).

Conclusion: Felmale gender maybe is a significant factor to enhance aminiglycosides-related nephrotoxicity. Additionally, the nephrotoxicity that associated with aminiglycosides was mild and reversible in long-term MDR-TB treatment.

PC-100267-14   Comparing the early treatment outcomes of MDR-TB in a decentralised setting with a centralised setting

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Background: Prolonged hospitalisation for the treatment of patients with multidrug resistant TB (MDR-TB) is neither possible nor effective in a low-income setting with a high burden of TB and HIV. Alternate models of treatment need to be developed and evaluated. In KwaZulu-Natal, South Africa, the centre of the TB and HIV epidemics, a decentralised model of treatment is being piloted at four sites within the public health services. This study aims to compare the effectiveness of the decentralised model with a centralised model. Preliminary data from this ongoing study is presented.

Method: This is a prospective cohort study. Data was collected from patients' clinical records using a standardised data extraction tool. MDR-TB patients over 18 years old were included from the decentralised sites and for the centralised group if they originated from districts without a decentralised site. Early outcomes were culture conversion and mortality. To compare treatment models, data was analysed using STATA.

Results: 861 patients were enrolled to date; 420 in the decentralised and 441 in the decentralised groups of the study. Subjects were followed for an average of 190 days per person (range 25–515 days). Baseline demographic and clinical characteristics were similar in both study groups. Time to treatment initiation was shorter in the decentralised sites; 89 days (range 32–491) compared to 109 days (range 30–443) at the centralised site. Time to culture conversion was 8.5 months in the decentralised sites compared to 24.5 months at the centralised site. All 95 patients who died were HIV positive; 9% died before treatment started and a further 22% within the first 30 days of treatment.

Conclusion: Preliminary data suggests that treating MDR-TB patients in a decentralised setting significantly improves the culture conversion rate and suggests decentralised treatment within the public health service is an effective model of treatment.

POSTER DISPLAY SESSIONS

DOTS: PUBLIC-PRIVATE MIX

PS-100128-14   A public private mix project in Howrah improves TB case detection

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Setting: Four large urban slums in Howrah, India.
Background: TB patients in these slums are treated either in public health facilities that cooperate with the Revised National Tuberculosis Control Programme (RNTCP) or by private practitioners (PPs). The PPs usually don't follow the International Standards for Tuberculosis Care.
Objective: To improve the case notification rate of the said slums through the involvement of the PPs in the RNTCP and the enrollment of their TB patients in RNTCP treatment schemes.
Methods: We established a public private partnership between the RNTCP and the PPs and evaluated its impact on the case notification rate in the project area. We compared the project area with an adjacent control area without such a partnership in terms of case notification.
Results: In the first four years of this partnership, the annualized total case notification rate of the project area improved by 6.4%, while it declined by 20.3% in the control area. The comparison of the case notification in both areas showed a statistically significant positive trend in favor of the project area ($P < 0.001$).
Conclusion: The involvement of the PPs in the urban slums of Howrah in the RNTCP results in an improved case notification rate in the project area.

PS-100155-14   Assessment of the involvement of private health care providers in DOTS in Khartoum State, 2009

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Tuberculosis (TB) control services including DOTS programme in most low-income countries have been planned and designed almost exclusively by National TB Programme (NTP) and implemented through the available network of public health services. Most countries however have two major sets of health care providers, public, owned by the State and private, comprising a range of institutions and individuals. Private health care providers play a significant role in health in Sudan; particularly in Khartoum the most condensed State. The objective of this study was to assess the involvement of private chest physicians, internal medicine physicians, general practitioners and physicians in charge of private hospital casualties in DOTS in Khartoum State, in terms of their knowledge about TB/DOTS, practice towards TB, and perception towards the NTP/DOTS strategy. The study was conducted in Khartoum State, involving 214 of the private health care providers. It is a descriptive, cross-sectional facility based study. An interview was done through a structured questionnaire for collecting data after pre-testing. Out of the 214 interviewed, 18.7% have good knowledge about TB/DOTS, 53% of them use sputum test for TB diagnosis. 66 out of the 214 treat TB patients in their clinic and 60.6% out of the 66 are not in-line with TB treatment guidelines. Few of the private health care providers adhere to sputum test in following up of the TB patient. Almost half of them have a perception of in familiarity with the NTP. Knowledge of private health care providers regarding Sudan NTP and DOTS strategy was poor and they were not following recommended guidelines for control of Tuberculosis, but they were willing to participate and get involved in the future. More exploration is needed to conduct and strength PPM in Sudan.

PS-100171-14   Referral conformation for tuberculosis patients referred from private health facilities to public health facilities

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Aim: TB referral box is a good entry point for PHSP-Ethiopia to strength the referral linkage between public and private health facilities and also creates a good opportunity to trace TB patients and to strength transfer out feedback for TB patients referred from private health facilities. We determined gap between the referral date and started treatment following TB diagnosis.
Methods: A cross sectional Structured checklist were prepared to assess patients registry and TB referral sheet from fourteen health facilities to identify the gap between the referral date and the started treatment, correct category, diagnosis, regimen, age/sex correctly recorded and the data were analyzed.
Results: Among 14 health centers, only six had trained providers on TB-HIV. From 119 all forms of TB cases, 29 (7.3%) are P/POS cases, 55 (46.2%) cases are females, among Female TB cases, 13 (23.6%) cases are P/POS. The median age was 30. The majority (82.35%) of patients' referral sheet were correctly registered. 6 (5.05%) TB patients' age were not properly registered, 4 (3.36%) cases sex were registered incorrectly. 8 (6.72%) cases were registered misdiagnosed and

3 (2.52%) cases referral date not written on the referral sheet. In all visited health facilities referral feedback mechanism non existence. On average the referral date and the date on which patient started treatment was 2.96 the range was 0–31. On average referral date and the date on which Female TB patient started treatment was 3.45, whereas on average referral date and the date on which male TB patient started treatment were 2.58. Seventy seven percent of TB patients were started their anti-TB drug on less than six days whereas twenty three percent of cases were delayed greater than five days to start the treatment.

Conclusion: The main problem observed from this finding was the gap between the referral date and started treatment is very prolonged, the range was 0–31 days.

PS-100222-14   Tuberculosis case management in hospitals in West and Central Java, Indonesia

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Background: Since 2005 hospitals are involved in tuberculosis (TB) control in Indonesia. This study aimed to obtain information on quality of TB case management in hospitals that have implemented the DOTS strategy.

Design/methods: A cross-sectional study was conducted involving 8 hospitals (public, private, teaching, and pulmonary hospitals) in West and Central Java. TB notifications and treatment results of TB patients from hospitals and primary health care clinics (PHC) in the two provinces were collected. A qualitative study was performed to collect information from patients, treatment observers, and health care staff on the implementation of the DOTS strategy.

Results: In 2007, 52 413 new TB cases were notified, of which 10% were notified by hospitals. The average treatment success rate of smear-positive TB cases reported by PHC (94%) was significantly higher than the treatment success rate reported by hospitals (67%). The treatment success rates varied across hospitals. The overall success rate of smear-positive TB cases was 61% in West Java and 73% in Central Java. Less than 50% of TB cases diagnosed in hospitals were registered in the DOTS unit. TB cases registered in the DOTS unit received standardized treatment (OAT) in most hospitals, but not all cases who received OAT had a treatment observer. Problems related to DOTS implementation in hospitals were lack of internal linkage, and very limited health education to patients and treatment observers.

Conclusion and recommendations: This study shows that improvement of TB case management in hospitals is needed to ensure that patients receive proper diagnosis and treatment.

PS-100375-14   Typical survey on TB diagnosis, treatment and management in two TB hospitals in China

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Aim: TB hospital play an important role in TB control in China. The result of the survey on TB diagnosis, treatment and management in TB hospital will helped to develop strategies.

Methods: Using typical survey method, selected two TB hospitals, looked up all the case history in 2007 and implemented telephone interview in part of the patients.

Results: Out of 374 cases, 228 (61%) were male, the average age was 42.7, 188 (50.3%) cases were complicated with other diseases. The ranking of the diagnostic criteria were: X-ray, clinical symptom, CT, sputum smear examination, sputum culture examination and pathology. X-ray, clinical symptom and CT were the main diagnostic criteria in the two TB hospitals ($P < 0.05$). Duration of hospital stay 334 (89.3%) cases were prescribed second line anti TB drugs, and the average length of stay in hospital was 44.5 days. After hospital discharge 192 (51.3%) cases were continued under the outpatient treatment, 30 (8.0%) cases were transferred to the TB dispensary, and 152 (40.6%) cases defaulted.

Conclusion: The poor implementation on TB diagnosis, treatment and management in TB hospital will lead to the high default rate and the high drug resistant rate. So we need to establish ISTC manual as soon as possible, all the TB patients should obtain the standard care.

Table   Diagnostic criteria in the two TB hospitals in 2007

	Diagnostic criteria					
	Sputum smear	Sputum culture	Pathology	X-ray	CT	Clinical symptom
Cases	96	45	3	290	150	274
% in all cases	25.7%	12.0%	0.8%	77.5%	40.1%	73.3%
% in all diagnostic criteria	11.2%	5.2%	0.3%	33.8%	17.5%	31.9%

PS-100544-14   Evaluation of the pilot project of PPM DOTS in Afghanistan

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Challenge: To identify the adequate models of PPM for NTP to involve Private Practitioners (PP) and providing information for developing National Guideline in Afghanistan. 36 PPs in Two convenient sites (Mazar & Kabul cities) were selected for this pilot.
Intervention: After mapping and consultative workshop, the private practitioners (PP), those agreed to engaged, were selected and trained in DOTS. The role of PPs was to identify TB suspects and diagnosis, treat and refer them to the designated core health facility. Data were collected from the applied suspect register and TB registers books.
Results: Totally, 545 TB suspects had been identified, among them 343 (63%) had been actually examined for direct smear examination. The laboratory result of 52 (15%) of them were positive for TB. The diagnosed cases were higher in Mazar (71%) city then Kabul (55%). The proportion of TB cases among gender; 16 (39%) were male and 25 (61%) female.
Conclusion and recommendation: This pilot has contributed to increment of case findings, especially in Mazar, resulting in about 8% increment of case notification. Since previous study indicated people's preference of private sectors as first contacts. Thus, these pilots proved that PPM might have beneficial impact on case findings in Afghanistan. However, there have been several problems to be solved and the biggest one is high rate of early defaulters. Although complicated health seeking behavior attributed to this, functioning referral system specific for PPM should be developed.

PS-100620-14   Determining factors of TB suspect finding by private practitioners in Bali, Indonesia, in 2008

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Background: Survey of tuberculosis (TB) prevalence in 2004 shows that proportion patients with TB suspect symptoms which were looking for treatment to public health center (60%), private practitioners (PP's) (52%), government hospital (40%), private hospital (16%), midwife (10%) and self treatment (10%). In Bali, the PP's contributions to TB suspects identification still low, the average was 2.8%.
Objective: To identify factors that could be related to PP's contribution on TB suspect referral to public health center.

Methodology: A case control populations based was applied. Sample consists of 100 cases and 100 controls. Criteria to be case or control groups were based on whether they referred at least 1 TB suspect to the public health center since 2006. Data analyzed by bivariate and multivariate using logistic regression.
Results: Base on multivariate analysis found determining factors that could be related to PPs contribution on TB suspect referral to public health center were male PPs had more contribution, PPs that supervised by DOT Official had more contribution, PPs that had TB suspect form referral had more contribution and PP's practice that <5 km to nearest laboratory for smear examination had more contribution (Table).

Table   Result of multivariate analysis on determining factors of TB suspect finding by private practitioners in Bali, Indonesia, in 2008

No	Variable	Wald	Sig.	Exp(B)	CI (95%)
1.	Gender	5.111	0.024	2.042	1.10–3.79
2.	Health worker supervision to PPs	4.154	0.042	2.143	1.03–4.46
3.	Availability of referral form	10.483	0.001	2.785	1.49–5.18
4.	Distance to laboratory	6.155	0.013	2.161	1.18–3.97

Conclusion and recommendation: The factors that associated with TB suspect referral are socialization about the DOTS strategy, Supervision by DOT Official, availability of TB suspect referral forms, closeness to laboratory that can perform smear examinations. We suggest that all PPs should receive high quality socialization about the DOTS strategy, continues supervision of the PPs and provision of TB suspect referral forms, provide fixation of smear examinations in satellite public health center.

PS-100621-14   Program implementation

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Methods: India is the highest TB burden country, where Private Health Sector contributes substantially to Primary and specialized health care. There are about 170 000 Qualified Doctors working in the Private Health Sector. Private Health Care Sector in India accounts for:
- 83%, out of Pocket expenditure,
- 75%, of the total ambulatory care,
- 66% of Inpatient care,
- Treatment of >45% of all the TB Patients.

Sensitization and Training of Doctors engaged in Private Health Sector in RNTCP based on DOTS is made through CMEs (Clinical Meetings). Public Health Project funded by the Government of India provides FREE diagnostic tools and Medicines to all TB Patients.

Results:

Population of Project states (Six States): 385 690 753

Total IMA Membership of Doctors: 58 864

Period of Project Study One Year: (April 08 to March 09)

Doctors Sensitized: 12 090

Doctors Trained: 2546

DOT Centers Opened in Private Sector: 803

Conclusion: Involvement of all health providers is absolutely crucial to the success of Stop TB Strategy.

PS-100650-14 Situation of private laboratories performing sputum for AFB microscopy in Yangon, Myanmar, in 2009

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Setting: Yangon, city of Yangon Division, Myanmar.
Objectives: To explore the situation of private laboratories performing sputum for AFB microscopy.
Design: A cross sectional study was conducted from August to December, 2009. Yangon has 62 private laboratories. Structured interviews were conducted with in-charges of private laboratories.
Results: 428 staff were working in private laboratories and only 12.6% said they had been trained on sputum for AFB microscopy. Out of staff interviewed in public laboratories, 73.5% were part time staff and also working in public sector. Thirty three percents of staff working in those laboratories were medical technologists. The laboratories opened almost every day (mean 28.9 days and mode 30 days). The private laboratories had average of 14 working hours a day. Sixty eight percents of private laboratories had binocular microscopes, 26% had monocular one and 6% had none. Sputum for AFB microscopy was performing in 92% of private laboratories assessed. Total average attendance was 564 per month and sputum smear slides for AFB examination was 47 per month. Average cost for one sputum smear was 1055 Kyats (1 US$). All private laboratories are not under quality control umbrella of National Tu-

berculosis Programme (NTP). In-charge of the private laboratories expressed their willingness to involve in TB control (70.9%).
Conclusion: The findings urge for the involvement of private laboratories under public-private mix scheme of NTP by advocating on current concept of TB diagnosis, providing appropriate training and resources and establishing the strong referral linkage between private laboratories and NTP.

PS-100718-14 TB case-finding intensifies with involvement of private providers in the slums

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Setting: Three informal settlements (slums) in Nairobi, Kenya, where there is a lot of TB due to overcrowding, malnutrition and poverty.
Objective: To show the contribution of small private providers in intensifying TB case finding in slums.
Methods: 302 drug shops and clinics in 3 slums have been referring clients with signs and symptoms of TB to diagnostic sites after training on basics of TB, from January 2009. Referral forms from providers were analyzed for suspects found to have TB, validated by the AFB and TB register. New TB patients registered in 2008 before the initiative begun, was compared with 2009.
Results: A table showing increase in TB case finding after involvement of private providers is shown below.

Slum	2008		2009		2009		% increase in case finding	% increase in smear-positives
	New TB cases registered	Smear-positive	Referred suspects found with TB	Referred suspects smear-positive	New TB cases registered	Smear-positive		
Viwandani	452	220	118	46	529	229	16	4
Kiambiu	764	392	58	30	860	451	13	15
Mathare	528	194	88	26	580	204	10	5

Conclusion: Private providers including drug shops and small clinics in the slum play a significant role in intensified TB case finding, thus reducing diagnostic delays.

PS-100747-14 Current TB control practices in selected hospitals and private clinics in Myanmar

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Setting: Before the introduction of International Standards for TB Care (ISTC) in Myanmar, assessment

survey was conducted in 20 selected sites involving general hospitals (8), Universities of Medicine (2), private clinics (6) and township health departments (4).

Objective: To assess current TB control practices of medical doctors in different settings.

Method: A cross sectional survey by using open ended structured questionnaires was conducted.

Findings: Total of 98 doctors, 48 from General Hospitals, 27 from University of Medicine, 15 Private Practitioners and 8 from Township Health Department were interviewed. Fifteen percents of doctors from hospitals defined TB suspect with cough for 4 weeks and above. For the diagnosis of Extra Pulmonary TB, 50% were taking biopsies for histopathology. Forty-five percents of doctors determined sputum smear negative TB with positive CXR. In area of diagnosis of TB in symptomatic children, 69% of doctors forgot to ask history of exposure to an infectious TB patient. Forty-two percents were not done follow up sputum examination to the pulmonary TB patients. For the monitoring of progress during treatment, 22 out of 98 were using CXR. Only 46% of doctors initiated TB patients to do VCCT. Majority of doctors were not being asked a contact history for likelihood of DR-TB. Only 48% of doctors are familiar with DR-TB treatment. Only 53% of doctors are being done contact evaluation.

Conclusion: Some of the important international standards are differing from the real practices. Adoption, dissemination and provision of training on ISTC to care providers are crucial in TB control in Myanmar.

PS-100749-14   Identifying all tuberculosis cases detected in the health system: a new approach to revisit the case detection rate

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Background: In Afghanistan, private or public health facilities outside of NTP are often first contacts for TB cases. Thus, performance of those facilities, regarding reporting or referring, greatly affect case detection. The aim of this study is to determine the case detection rate based on the extent of reporting/under-reporting rate of non-NTP providers. This rate will be used to estimate the total number of cases and TB incidence.

Methods: A prospective cohort study was carried out during the period (third and fourth quarter of 2008) in the selected three provinces (Parwan, Baghlan and Jawazjan). For all non NTP health providers (private hospitals, private clinics, pharmacies), a modified TB suspect register was introduced. Each suspect and confirmed case was traced back at the NTP records to determine the status of registration to define the proportion of cases detected by NTP.

Findings: Totally 845 TB suspect were identified in 169 non-NTP facilities. More than half (77%) of those TB suspects had been referred for examinations, but finally 498 (69%) suspects were registered as TB suspects at NTP facilities and among them 161 were diagnosed as TB. This represents 13% of TB cases among 1227 TB cases during this period.

Conclusion: The notified cases by non-NTP facilities could contribute to increment of the notification rate indicting the significance of involvement of non-NTP health care providers into TB control. However, simultaneously, it is crucial to prevent early defaulters.

PS-100777-14   Involving private pharmacies in urban DOTS program: preliminary report from Chennai

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Background: The study was done to evaluate the dispensing practices of anti-tuberculosis drugs by private pharmacies and the feasibility of involving them in DOTS (Directly Observed Treatment, Short course) program between April 2006 and August 2007 in Chennai city, India.

Design: Among the 1925 pharmacies registered under the Pharmacy Association of Chennai under 10 Corporation zones, 402 pharmacies selected by stratified sampling technique from 4 zones were interviewed with a pre-tested semi-structured questionnaire. They were then sensitized on their role in the DOTS program through workshops and one to one visits and were invited to contribute to the program by educating patients and by referring patients to appropriate treatment facilities.

Results: Among the 402 pharmacies, 89% of the pharmacists were aware of the symptoms of TB and 48% were aware that TB was diagnosed by sputum examination. While 90% of the interviewed pharmacies were dispensing anti-TB drugs, only 27% of them knew about the DOTS program. However, almost all of them were willing to participate in the DOTS program. About 101 TB suspects were referred from 64 pharmacies in the 1-year period following their sensitization.

Conclusion: Private pharmacies play a key role in influencing patients' treatment choices and in guiding them to appropriate health care facilities. This role becomes more important in tuberculosis control considering numerous treatment options available to patients. This study has demonstrated that pharmacists can be effectively used for case referral and the National TB control program needs to respond to them positively.

PS-100854-14   Strengthening partnership and referral: public and private TB-DOTS health facilities in Ethiopia

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Background and implementation challenges: The USAID| Private Health Sector Program (PHSP) led by Abt Associates support implementation of PPM-DOTS service in 95 private health facilities in Ethiopia. Public health facilities were unwilling to accept referral from PPM-DOTS sites directly rather they were repeating all the diagnostic procedures again which will incur additional cost and delay treatment initiation.
Intervention: PHSP in collaboration with Regional Health Bureau's conducted 13 Referral Advocacy workshops event (Jun–Oct, 2008), and 963 participants, district health officials, medical directors and TB nurses from public and private health facilities, get list of PPM-DOTS facilities and oriented with the PPM-DOTS guideline. Agreed action plan was developed to strengthen the referral networking. PHSP develop and distribute Referral Log were referred patients information's recorded. To track referred patients attendance small boxes distributed to selected 63 public health facilities to collect referral slips from PPM sites.
Results and lesson learned: Currently, there is no complaint of rejecting referrals from the PPM-DOTS facilities, rather PPM sites involved in program review and benefited from supportive supervision, mentoring and laboratory quality assurance scheme. Furthermore, the PPM-sites are treated as public facility in logistic supply. Referred patients were quite high 10 809, compared to 3311 case holding (Jan–Dec 2009). The referral attendance assessment shows out of 1114 selected patient for confirmation 923 were attended.
Conclusions and recommendation: Creating strong referral networking and partnership have significant importance in building confidence, trust and shared responsibilities between public and private sector. It is a key strategy that is highly suggested for successful program implementation and sustainability.

PS-100877-14   The challenge of confirming TB referrals: best practices from the USAID|Private Health Sector Program

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Background and challenges to implementation: USAID|Private Health Sector Program in partnership with the Ethiopian Ministry of Health has initiated Public Private Mix-DOTS in November 2006. A total of 96 private clinics provided TB treatment for 6625 patients as of December 2009. From January to De-

cember 2009 alone, private clinics referred a total of 10 809 TB patients for treatment. Tracking referred TB patients was a particular challenge.
Intervention or response: In December 2008, the project developed referral log book and a referral slip collection system. Referral slips collection boxes were distributed to public health facilities. Advocacy meetings were held with program mangers and providers in surrounding public facilities.
Results and lessons learnt: A rapid assessment was carried out in Western Oromia, 300 KM from the capital city of Ethiopia. This assessment was done in four of the 10 commercial clinics in Wester Oromia which accounts for 98% referred in the zone. From January to December 2009, the four clinics referred a total of 441 TB patients to 50 public health facilities. Data collection, however, was possible for 101 patients that were referred to 12 public health facilities that are located within 20 to 90 KM radius. Of total referred patients, 31 (30.7%) were sputum positive while the remaining 70 (69.3%) were other forms of TB. 79 of 101 patients (78.2% of the total) were confirmed reaching referred facilities. Twenty two of 31 (70.9% of the total) sputum positive patients were effectively linked.
Conclusions and key recommendations: Confirmed TB referral is remaining as challenge in the national TB control program. Private clinics are now making a significant contribution to TB diagnosis and referral. Confirmed TB referral; especially among sputum positive TB patients has public health importance.

PS-100901-14   Empowerment of Tuha Peut (local community leaders) for tuberculosis control in Aceh, Indonesia

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Background: In 2009 there were 2955 new cases of TB out of 4.67 million populations in Aceh. The main problem in controlling TB in Aceh is low TB suspects coverage and Case Detection Rate (CDR). This study aimed to increase TB suspect coverage by involving local community leaders (Tuha peut) and to assess the effectiveness of Tuha Peut in increasing TB knowledge in the population.
Methods: We adopted a quasi-experimental study design. Two separate districts were selected (Bireuen as an intervention group and Aceh Besar as a control group). Every district in have Pre group and Post group. Sample size in each group 210 responden. Tuha Peut in intervention area were engaged in TB control program. A structured questionnaire was applied to assess the knowledge change in the population.

Result: The incremental TB knowledge in intervention group was significantly higher compared to control group different ($P = 0.003$). The trend of TB suspect visiting primary health centre (PHC) increased in the intervention group. The number of TB suspected cases visited PHC before the intervention were 64 cases, meanwhile in 3 months after intervention there were 112 cases TB suspects registered in PHC.

Conclusion and recommendation: Involvement of Tuha Peut for TB control in Aceh increased public knowledge which led to increasing number of visits by TB suspect to PHC. Thus, Tuha Peut can serve as a model of community empowerment for TB control.

PS-100932-14   Public private mix in TB-HIV prevention and control: pilot project in Nelson Mandela Metro, South Africa

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Aim: TB has traditionally management been a public sector role. With increasing TB caseload due to HIV, poor referral systems, and scarce human resource within the public sector, the need for involvement of Private Practitioners (PP) has never been greater.

Methods: Care Dynamic Networks, a strategic partnership with ProHealth Wellness Clinics, NMM PPs, the Department of Health and Walter Sisulu University was set up in Jan 2009.

Training and Infection Control risk assessments were conducted. Drugs and sputum examination is provided by public system, while X-rays by private radiologists. A peer review mechanism (weekly clinical meetings) is in place. PPs assist in public clinics to review complicated cases.

Results: Seventeen (7%) of the 250 PPs in NMM are involved. The Table summarizes results from May 2009 to Feb 2010.

	Number (%)
TB patients enrolled	100
Smear + (Category I)	26 (26%)
Smear + Re-treatment (Category II)	3 (3%)
Smear + MDR (Category 4)	5 (5%)
Smear + XDR (Category 4)	2 (2%)
Smear negative PTB (Culture+/CXR suggestive) (Category I)	34 (34%)
Smear negative, Re-treatment (Category II)	1 (1%)
Smear negative, EPTB	24 (24%)
Smear negative, EPTB XDR (Category 4)	1 (1%)
TB patients tested HIV+	58 (58%)
Started on CPT	58 (58%)
Started on ART	33 (57%)

Challenges: Referral networks need strengthening especially within public sector. ARVs are not free within private sector, so a TB-HIV co-infected patient who cannot afford ARVs is managed under 2 different systems. Referring of TB contacts of PPM patients for screening in the public clinic overburdens an already overstretched health care system.

Conclusion: PPM approach is a promising option in achieving the strategic targets of TB-HIV.

PS-100985-14   Decongesting public diagnostic centers in central province

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Introduction: TB diagnosis is free in public laboratories in Kenya, country with a high burden of TB. Most TB suspects therefore prefer these public facilities causing congestion thus delayed diagnosis.

Objective: To decongest the few public TB diagnostic facilities in Central province, by involving private laboratories.

Setting: Three districts in central province which previously relied heavily on the district hospitals for TB diagnosis.

Methods: Provider mapping of all private laboratories in these district was done. The laboratories were assessed for engagement; staffs trained on sputum smear microscopy and commodities for TB diagnosis was provided. Twenty private laboratories started TB diagnosis in 4th quarter of 2009.

Results: A Table showing comparison of public labs before and after private engagement is seen below. The number of suspects in the district hospitals 4th quarter 2009 reduced by 48% after involving private laboratories.

Table Comparison of public laboratories before and after private engagement

| | Public laboratories (4th quarter) | | | | | | |
| | 2008 | | 2009 | | 2009 | | % |
District	Suspects	Positive	Suspects	Positive	Suspects	Positive	decrease
Karatina	755	120	69	14	507	15	91
Nyeri	332	41	271	53	87	35	18
Thika	510	142	489	93	316	78	2
Total	1597	303	829	160	547	128	48

Conclusion: The burden of TB diagnosis can be reduced in the public laboratories by engaging the private sector in TB diagnosis.

PS-100995-14   Convergence of public health institutions for TB care: a project experience

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Setting: Hyderabad Urban DOTS Project (HUD), a TB initiative of Bhagwan Mahavir Medical Research Centre (BMMRC) supported by Central TB Division, GFTAM and TB Alert India. HUD implemented TB interventions from February 2005 to January 2008 in Hyderabad Urban District, Andhra Pradesh, covers population of 5 Million.

Objectives:
- Increase access to primary health care for TB in the Public Health Institutions
- Increase Intra-departmental and inter-departmental co-ordination for TB control

Methodology: Project worked closely with, Public and Private Sectors and conducted capacity building activities for TB including Continuous Medical Education, Modular Training, Sensitisation programmes and individual interactions. The process of implementation, much to the fulfillment and expectations of the project, reflects the sustainable, replicable and cost-effective components, provided it is put in place through adjustments in the machinery of different departments.

Results:
- Project organised TB Sensitisation to 2200 private health providers (1654 Allopath & 1038 Non Allopath), 16 Corporators (local political leaders), 1654 Government Staff at Public Health Institutions, 872 Teaching & Trust Hospitals and 104 Corporate Hospitals
- The percentage increase in TB symptomatic's at Public Health Institutions (PHI) increased by 70.5% between 2004–2007
- The Case detection rate increased at PHI from 49.5/100 000 to 67.5/100 000 from 2004–07
- Total number of patients diagnosed and placed on treatment were increased from 5739 in 2004, to 7147 in 2007

Conclusion:
- Convergence of primary care for TB Care in peripheral health institutions–Urban Health Posts (UHPs)
- Creation and development of secondary care hospitals equitably in urban area, keeping in view of future expansion of city
- Back and forth referrals of patients from secondary care to tertiary hospitals
- Accountability at all levels through process indicators

PS-101039-14   Evaluating financial burden for TB patients in three PPM approaches in China

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Background: China's PPM mainly refers to the collaboration between TB dispensaries and public hospitals, including TB dispensary approach (TDA), special TB hospital approach (THA), and designated hospital approach (DHA). Patients treated in public hospitals experienced high medical costs. This study compared patient financial burden in different PPM approaches.

Methods: Six sites at the county/district level of different PPM approach in four provinces were selected through stratified sampling. Patient survey and outpatient chart review were conducted with 293 new TB patients without any complications/resistance that were registered in 2007 and finished treatment by July 2008. Government policy papers and hospital documents were employed as well.

Results: Patients experienced serious financial burden during the healthcare seeking process. On average, a TB patient spent 6118 RMB on TB related treatment. Patients in THA had the highest overall total costs (RMB 11 626) and hospitalization rate (83%). In TDA, the results were mixed. One TDA site had a relatively high hospitalization rate (65%) and medical cost (RMB 7179), while results were low in the other site. DHA witnessed the lowest hospitalization rate (15%) and medical costs (RMB 5307). In THA and the high costs site of TDA, over 80% of hospitalization and 50% of medical costs occurred in the period between TB diagnosis and DOTS treatment.

Conclusion: The study indicated that most TB patients had serious financial burden during the healthcare seeking process. DHA had the lowest patient costs while THA the highest. The majority costs were due to hospitalization in general hospitals and TB special hospitals during the period between TB diagnosis and being referred to TB dispensaries to receive DOTS treatment.

PS-101293-14   Issues and challenges to PPM and ACSM: multi-country assessment from Eastern Mediterranean Region

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Background: This study was done to document Public-Private Mix (PPM) experiences with special emphasis on advocacy, communication & social mobilization (ACSM) in six countries of the region.

Design: Review of the structure and spread of health care delivery especially the private sector and the existing PPM interventions and field observations.

Results: Following models identified 1) Public-Public: NTP with department of Jails, Police, Military etc 2) Public-semi Public: NTP with Insurance, parastatal organizations 3) Public-Private (non profit): NTP with NGOs managing DOTS 4) Public-Private (for profit): NTP-private practitioners.

Issues and challenges: Few ACSM initiatives specific to PPM found. Pakistan in social franchise model expects partners to conduct ACSM for PPs while Yemen asks PPs to do it for themselves. Other countries do not have any strategic directions on PPM promotion while some countries don't even have the broader ACSM or PPM strategy. Human resource and capacity for both initiatives is deficient across the region. Policy and integration issues in the area identified yet strong felt need of ACSM specific to PPM was also there.

Possible interventions to address challenges: There is a need to develop a clearly spelled out communication plan to promote PPM. The plan should: keep PP's interest; have a careful mix of mass media and on-ground communication; and focus on introducing PP to the community. Activities like Seminars for local level advocacy and one-on-one sensitization meetings with PPs, free health/chest camps at the PP's facility; effective Client Provider Interaction and Involvement of community health should be scaled up.

PS-101147-14　Cost accounting of tuberculosis control services incurred by designated TB hospitals in China

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Background: As a part of PPM DOTS, some public hospitals are designated to provide TB care since 2007 in China. The new services provided by these hospitals requires more resource (such as more staffs and more lab equipments) to support than before. So how to finance for these hospitals to provide the new services is a very important question for policy-maker. And it is the first step to account the additional cost of TB control incurred by these hospitals.

Objective: To describe cost of TB control incurred by designated TB hospitals.

Method: 4 designated TB hospitals of county level in 4 provinces were interviewed using structured questionnaires in China. The whole cost and ladder apportionment of expenses methods were employed to account cost of TB care and control incurred by these hospitals.

Results: A total of 4 hospitals were interviewed on the basis of typical survey in 2009. In 2008, the management cost per visit of TB patient on average is ¥33.30 with none income by charge. The diagnosis and treatment cost per outpatient visit of TB patients on average is ¥149.83 with the income of ¥125.15

per outpatient visit by charge. The average inpatient cost of TB patients is ¥9037.68 with the average income of ¥6482.03 by charge. So the deficit of TB management is ¥33.30 per visit of TB patients. The deficit of TB outpatient is ¥24.68 per outpatient visit and that of average inpatient is ¥2555.65.

Conclusion: For success of PPM DOTS, the deficit of TB control services incurred by hospitals should be reimbursed by other ways in addition to patients charge. Because the nature of TB management service is pure public goods, the deficit of ¥33.30 per visit should be reimbursed by government budget. And the deficit of ¥24.68 per outpatient visit and that of ¥2555.65 per inpatient might be reimbursed by social medical insurance because it is a good way to balance the benefit between patients and designated hospitals.

PS-101349-14　PDA supervision tool helps to improve PPM-DOTS site performance

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Background: In 2007, Ethiopia's Ministry of Health began to promote Public-Private Mix for TB-DOTS. The USAID|Private Sector Program (PSP) helped launch a PPM-DOTS pilot in 20 sites. By July 2008, PSP supported 105 private and workplace PPM sites in 4 regions. PSP observed that supervision checklists could not be easily analyzed to identify problems across the program.

Intervention: PSP first developed an improved supervision tool. In late 2008, PSP converted the tool to a PDA application. This enabled staff to enter and analyze observation data in clinics. The PDA calculates facility scores for 10 TB clinic indicators plus 7 TB and 7 HCT lab indicators. Each indicator score combines several observation findings. The PDA reports indicators using red, yellow, or white color codes to indicate the urgency of the problems. Supervisors focus first on code-red problems.

Results: Data shows notable improvements in key indicators. A December 2007 PPM pilot evaluation found that 65% of the 60 professionals trained for the PPM-DOTS pilot had left their facility within the year. In Q4 2009, at least 82% of 91 sites retained the TB physician and nurse.

In 2009, annual treatment outcomes in 73 sites for 554 smear-positive patients reached 65.7% cured, 12.6% completed, 10.6% transferred, and 11.7% unfavorable outcomes. In 2008, PSP promoted HCT for TB patients. In Q1 2009, 30% of TB patients accepted HCT in the first treatment quarter. By Q4 2009, that number had risen to 57%. In one region, 70% of patients tested in the first quarter. In 2007, AFB EQA showed 17.5% of 120 slides sampled with discordant results. From Q1 2008 to Q3 2009, a total

of 2319 AFB slides assessed and only 2.9% of slides had discordant results.

Conclusions: The detailed supervision tool coupled with real time data analysis helped supervisors to target important problems and demonstrate improved performance over time.

PS-101505-14   The availability of ATBM in the private market in EMR countries and how to limit dispensing

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Methods: Structured questionnaires were administered to pharmacy depts. managers at MOH, NTP staff were interviewed ,moreover field visit survey was done on 140 private pharmacies of the 14 countries of 22 EMR countries during the regular WHO/GDF visits 42 NTP staff were interviewed as well; the questionnaire was about to confirm the presence of 1st line ATBM in the private market, to explore the different types of ATBM in the private market with the reference to dosage form, combination and concentration/strength, Comparing the findings of the survey with the treatment guidelines of WHO and NTP, To get an insight about the level of education on TB issues and handling of TB patients by pharmacists.

Results: Among 22 of EMR countries; 8 of them (36%) had no response, the rest; 14 countries (64%) the result was; ATBM were present in all pharmacies visited for the survey in 9 (64%) of them, where the type of medicines present varied between RHZE and their combination with different strengths and dosage forms. Prescribing of ATBM was usually targeted towards treating TB and not other conditions requiring anti-bacterial. OTC dispensing by pharmacists is happening but not frequent. Level of education about ATBM is generally low. Level of knowledge about dangers of irrational use of ATBM was generally low.

Conclusion: EMP/ STB/EMRO decided to have regulatory action for ATBM available in private pharmacies which might: advise governments (MOHs) to investigate the possibility of negotiations with pharmaceutical manufactures of ATBM to adjust concentrations according to WHO recommendations, to advise governments on de-registration of those medicines that are present in the market and not complying with the global clinical and WHO recommendations, limiting the presence of ATBM to primary health care clinics in rural areas and primary health care hospitals in urban areas. Investigate with governments enforcing sanctions on private pharmacies were ATBM are present.

Country name	Country response
1 Djibouti	No procedure for registration of medicines so far/No regulation for TB medicines present
2 Iran	List of registered medicines received/only 5% of TB medicines are available in the private market 'under review for complete ban'
3 Jordan	List of registered medicines received/ No regulation
4 Oman	List of registered medicines received/Copy of decrees regulating availability of anti-TB medicines was also received
5 Tunisia	List of registered medicines received/ No regulation
6 Yemen	List of registered medicines received/ No regulation
7 Lebanon	List of registered medicines received/ No regulation
8 Sudan	List of registered medicines received/ No regulation
9 Pakistan	List of registered medicines received/ No regulation
10 Bahrain	No list received however Anti-TB medicines are banned/No copy of the regulation received
11 Iraq	List of registered medicines received/ No regulation
12 Somalia	List of registered medicines received/ No regulation
13 Afghanistan	No response
14 Libya	List of medicines received/ No regulation
15 Qatar	No response
16 UAE	No response
17 Syria	No response
18 Egypt	List of medicines received/ No regulation response
19 Kuwait	No response
20 Morocco	No response
21 Palestine	No response
22 Saudi Arabia	No response

IMPROVING COORDINATION AND LINKAGES OF TB-HIV PROGRAMMES

PS-101434-14   How to improve the fight against TB-HIV co-infection?

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Background: Mandela said 'We can't fight AIDS unless we do much more to fight Tuberculosis (TB)'. TB is the most common opportunistic infection and cause of death among HIV-infected individuals. Thus, to reduce the morbidity and mortality of these infections, better integration of TB and HIV services are essential to support provider-initiated HIV testing of all TB suspects.

Objective: To evaluate implementation of rapid HIV testing in patients with active TB and to describe the characteristics of TB-HIV patients identified in the study period.

Methods: From June to December 2009, in Paranaguá city with TB incidence of 102.3 per 100 000 hab, the TB Control Program coordination carried out a prospective study among newly TB cases diagnosed in a reference service, implementing HIV rapid testing.

Results: During this period, 85 TB cases were diagnosed and 84 (99%) were tested by HIV, being 20 (23.5%) with positive results. Refusal for HIV testing occurred in 1 patient. In 2008 that used non rapid HIV testing, the coverage of HIV testing was only 44%, with 14% of positivity. Among 84 TB cases, the median age was 36.8 years and 71% were male. Among 20 HIV seropositive TB cases, the median age was 43.5 years; 85% were male; 30% had incomplete primary education; alcoholism was mentioned by 35%, diabetes in 5% and drug addiction in 20%. Among 8 cases with known HIV positivity results, CD4 T cells greater than 350 was observed in 3 (37.5%), and among 12 with first notice of being HIV infected, CD4 T cells greater than 350 was observed in 8 (67%).

Conclusion: The use of the rapid test for HIV increased the coverage of HIV testing and seropositivity among TB patients, respectively from 44% to 99% and from 14% to 23.5%. The diagnosis of seropositivity in TB cases attended in a reference service occured a pre-AIDS phase. The engagement of TB Program to adopt tools to combat HIV-TB enabled the use of HIV rapid tests resulting higher effectiveness of HIV testing in TB case.

PS-100064-14   Priority for Local AIDS Control Efforts (PLACE) in Nigeria

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Background: The consequences of HIV/AIDS can be far-reaching for people. Not only does HIV disease have terrible consequences for the individual, causing serious illness and eventual death, it has the potential to trigger negative social reactions.

Method: Identification of (Priority Prevention Areas) PPAs- Mapping of PPA, Over 30 Venue Outreach Staff (VOS) were employed and trained by professionals to reach out to the hard to reach in the community through the just concluded PLACE project. Talking Drum was used as a cultural sign of love to entertain and draw people's attention to the message, cultural dance and drama was also organized to disseminate the HIV message.

Result: The rich people and politicians attend most of the PPAs for pleasure, the result shows that about 34% were afraid to do HIV test, about 12% of the people that did HIV test were positive within the community. This encouraged many of them to do the test to know their status, condoms was distributed after asking several questions on how they can be protected from HIV.

Conclusion: Since the hard to reach are easy to reach in clubs and night parties, i.e., Politicians, Bank man-

agers and Students etc. it is advised to support more of the HIV prevention projects in communities where people don't have adequate information about HIV/AIDS and introduce preventive methods.

PS-100316-14   Up-skilling of community care givers to provide comprehensive TB-HIV/PMTCT care, South Africa

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Background: Community participation in TB-HIV activities including Prevention of Mother-To-Child Transmission (PMTCT) is one way to increase access to diagnosis and treatment. The aim of this project was to up-skill community care givers (CCGs) to enhance the provision of TB-HIV/PMTCT integrated care at community level.

Methods: The study was conducted in Sisonke, a rural district of KwaZulu Natal (KZN). A participatory approach was used. Key program managers and TB and HIV/AIDS coordinators as well NGOs providing HIV/AIDS services participated in a district subcommittee established to design, implement and monitor the up-skilling program for CCGs. CCGs were trained on health education related to TB-HIV/PMTCT, screening for TB and sexually transmitted infections (STIs), home based voluntary HIV counseling and testing (VCT), TB and antiretroviral adherence and infant feeding counseling. Both Community Health Workers and Home Based Carers were selected based on their education level (grades 10–12) and their scope of work was harmonized.

Results: 47 CCGs were trained from October to December 2009. Multi-sectoral community mobilization events involving Chiefs/Induna, traditional healers, professional nurses and CCGs were conducted in 15 villages to introduce the program. CCGs provided VCT, TB/STI screening, TB sputum collection and referral to health facilities. A total of 1561 people attended, 393 (25%) were tested for HIV with with TB/STI screening and 19 tested HIV positive, all of whom had blood taken for CD4 testing. 19 (5%) were TB suspects and had sputum collected.

Lessons learnt: During community mobilization activities, key people in the communities such as chiefs and traditional healers were the first to access VCT which encouraged community members to be HIV tested. The high number of people that accepted HIV testing indicated the acceptability of CCGs to provide VCT with TB/STI screening in their own communities. This could be an avenue to reduce HIV and TB related stigma in the community.

PS-101324-14   How to reach the most-at-risk populations with a TB-HIV program in Zanzibar?

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Background: Most At Risk Populations (MARPs) in Zanzibar represent a high HIV prevalence group (16.0% among Injection Drug Users-IDUs, 12.3% among Men having Sex with Men-MSM and 10.8% among Female Sex Workers-FSWs; from Integrated Behavioral and Biological Surveillance Survey among Most at Risk Populations in Zanzibar, 2007, MOH/CDC), with overlapping risk behavior, and potential bridging with the general population; despite the relatively low TB prevalence in Zanzibar (<100/100 000), they are a group at higher risk to develop TB., In 2009, three local NGOs supported by ICAP reached 2339 IDUs, 297 MSM, 1104 FSW through education and HIV testing and counseling.

Intervention: Peer educators and outreach workers from the local NGOs and MKUTA, a national NGO composed by former TB-HIV patients will be trained on TB-HIV using the national curriculum. Selected IDU, MSM and FSW will be encouraged to be part of the pool of peer educators and outreach workers. TB-HIV messages will be integrated into the existing education program targeting MARPs and provide TB-HIV screening, care and treatment at community level, sober houses and dropping centers. TB drugs as well ART will be provided by the Zanzibar TB and Leprosy Program/Zanzibar AIDS Control Program to the treatment supporter, who will be responsible to supervise the entire course of the treatment.

Results: By the end of year 2010, over 150 peer educators and outreach workers will be knowledgeable on TB-HIV, weekly TB-HIV education sessions will take place at community level at 100 sites covering two islands-Pemba and Unguja, one phone health line will disseminate TB-HIV messages, 6000 individuals from targeted MARPs will be reached by local NGOs, 70% will be tested for HIV and screened for TB and eventually and estimated 10% of the average annual notified TB cases will be averted.

PS-100138-14   Improving the coordination and performance of TB and HIV interventions in Northern Uganda

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Background and challenges to implementation: Integrating HIV activities is a challenge for TB programmes. Before 2006, TB and HIV in Uganda were vertically managed by two distinct programmes with different funding sources, different staff operating in detached departments, different schedule of drug order and procurement and different recording systems. Relationships between the two programmes started in 2006 with dissemination of policy documents by the Ministry of Health recommending avenues for collaboration. The Northern Uganda Malaria AIDS and Tuberculosis (NUMAT) Program operates in 9 districts of northern Uganda, a region whose HIV prevalence of 8.2% is higher than the national average.

Intervention or response: NUMAT worked with the 9 districts and the TB regional office through multiple interventions including: training of health workers in TB-HIV collaborative activities; improved availability of TB drugs, reagents, HIV test kits and other supplies at diagnostic centers; integrated support supervision; technical assistance to conduct quarterly review meetings on TB-HIV; dissemination of educational messages to local leaders and general public. TB-HIV performance for the Northern Region from 2006 to 2009 was assessed using the existing reporting system.

Results and lessons learnt: HIV parameters were included in the TB cohort reporting and HIV information added to the TB registers. The proportion of TB patients tested for HIV steadily increased from 43% in 2006, to 67% in 2009. The percentage of co-infected HIV-TB patients stabilized around 50%. No information was recorded on cotrimoxazole prophylaxis therapy and anti-retroviral treatment (ART) for the co-infected patients in 2006. In 2009, 84% of co-infected patients were put on CPT and 21% on ART.

Conclusions and key recommendations: A shift from a vertical approach to an integrated collaboration is possible. However gaps remain and continuing support is needed to sustain achievements in the long-term.

PS-100141-14   La mutualisation des ressources en TB-VIH, une alternative à la rareté des financements

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Introduction : L'association LOUDON reçoit les financements du Fonds Mondial pour l'exécution des activités de prévention de la tuberculose. Avec ces mêmes ressources, elle s'est faite promotrice des activités de prévention du VIH/sida.
Objectifs : Encourager l'intégration programmatique pour une utilisation rationnelle des ressources et une pérennité des actions contre la TB et le VIH/SIDA.
Méthodes : Depuis 2005, les animateurs communautaires font la sensibilisation sur la TB sous la supervision des agents de santé. Grâce à l'incitation et à la modération par les animateurs, le thème du VIH est abordé par la population. En développant le thème, les animateurs exposent aux participants le lien TB-VIH. Au terme d'une animation, ils renseignent les outils de suivi suivant les canevas en TB. Les animateurs et les agents de santé superviseurs reçoivent sans majoration leurs perdiems malgré leurs interventions et le temps supplémentaires passés à discuter du VIH.
Résultats : 80% de la population du district a été mobilisée chaque année pour des causeries sur la TB et le VIH ; 60% des animations en prévention TB a connu l'intégration d'un sous thème sur le VIH ; L'association est impliquée par les autorités sanitaires aux actions de lutte contre le VIH au niveau local et régional ; Les interruptions de financement chez les acteurs VIH ont été moins ressenties par les populations du district sanitaire.
Conclusion : Cette pratique s'est avérée rationnelle et a permis d'atteindre l'aspect coinfection TB-VIH. Dans un contexte de rareté des ressources, elle constitue un modèle pour des acteurs qui ont à cœur la continuité des actions communautaires. Cependant, seules les données du district sanitaire ont permis ici d'avoir des statistiques spécifiques au VIH. De ce fait, le renforcement de l'association par la mise en place d'un système intégré de collecte des données TB-VIH est nécessaire.

PS-100330-14   Analyse critique de la prise en charge de la co-infection TB-VIH au Burkina Faso

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Cadre : Au Burkina Faso, la prise en charge de la co-infection tuberculose-Sida est un défi pour les acteurs des politiques et système de santé. Elle présente des enjeux psychologiques, socioculturels et biomédicaux. Les modalités de prise en charge sont balbutiantes.
Méthodes : Une approche qualitative incluant à la fois des entretiens individuels semi-structurés avec agents de santé, malades et leurs proches, acteurs communautaires, ainsi que des discussions collectives, et l'observation des pratiques de soins dans les centres de santé. Analyses socio-anthropologiques accompagnant un projet de santé publique dans des trois districts sanitaires de 2006 à 2008.
Résultats : Les malades font face à une double crainte : l'image sociale négative des deux maladies, et la lourdeur des traitements. Il y a un problème d'intégration sociale puisque leurs relations sociales sont mises en difficulté par des humiliations et la marginalisation sociale. Le malade présente un état psychologique déséquilibré avec des réactions impulsives et une résignation et la fatalité. La peur de la stigmatisation sociale liée à la co-infection chez les séropositifs au VIH retarde le diagnostic de la tuberculose malgré la chronicité de la toux. L'expérience douloureuse des antirétroviraux et antituberculeux crée une amertume face aux médicaments en plus des services de soins capricieux. La co-infection engendre une représentation négative de la vie et de la maladie. Le poids social et thérapeutique du sida engendrerait une négligence de la tuberculose, posant ainsi un délicat problème de santé publique.
Conclusion : La précarité économique et les marginalisations subies par les malades chroniques dans leur environnement débouchent sur une mise en difficulté de l'estime de soi des malades. Une dimension à promouvoir pour organiser mieux les adhésions aux traitements, améliorer leurs rapports sociaux, et leur condition de vie. Les médecins traitants doivent acquérir des compétences en la matière.

PS-101388-14   Impact of ruptures of inputs and ARV in the accession of tuberculosis patients to the activities of TB-HIV co-infection

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Framework: Rupture of inputs and ARV in health structures for taking over of cases of TB-HIV co-infection have very negative reaction on the accession of TB patients to VDC. In effect, the lost credibility is very difficult recoverable by the CSDT.
Objective: To assess the level of accession of TB patients to the achievement of HIV test without or with frequent breakdowns of inputs and ARV.
Method: Comparative study of accession of TB patients to the realization of HIV test function without or with frequent breakdowns of inputs and ARV. 10 CSDT started the project for co-infected TB/HIV in

2004 were chosen for this study. The two periods considered are: 2004: absence and 2009: breaks and frequent of inputs and ARV.
Results: The percentage of accession of TB patients to the achievement of test of HIV has declined from 96% in 2004 to 62.3% in 2009.
Conclusion: The non-respect of commitments kept of TB patients for screening of HIV and more particularly as regards the fractures of inputs and ARV have very negative impact on the accession of tuberculosis patients to the activities of co-infection TB/VIH in Kinshasa.

PS-100688-14   Impact of the expansion of NTP-based HIV care on TB outcomes in DR Congo

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Background and rationale: In North Kivu, in the east of DR Congo, a fragile state among the 22 TB highest burdened countries, with a low level generalized HIV epidemic, and facing huge resource constraints to reconstruct the health system, the IHC research program of The Union assesses the feasibility of using TB clinics to deliver 'Integrated HIV Care for TB Patients Living with HIV/AIDS'. The package includes Provider Initiated Counselling and Testing, CD4 count, Cotrimoxazole Preventive Therapy, pre-Anti Retroviral Therapy care, Anti Retroviral Therapy (ART), and is monitored through cohort analyses.
Hypothesis: Integration of HIV care at TB clinics does not hinder TB outcomes in 13 pilot centers.
Method: Impact assessment based on comparison of routine information systems data before and after intervention in pilot centers, and with centers in the province without intervention (control). Intervention started in June 2006.
Results: Patients on HIV care doubled every year, with cumulative survival rate on ART of 94%, 80%, 68% and 65% at 6, 12, 24 and 30 months respectively. TB case finding remained steady in both groups. Treatment success improved in pilot group, both compared to before intervention and control group.

	2005	2006	2007	2008
Pilot				
New TB cases	845	837	872	856
TB success	78%	76%	84%	89%
TB abandon	6%	8%	2%	3%
No on Pre ART	0	40	91	86
No on ART	0	45	100	190
Control				
New TB cases	2047	1847	1858	1953
TB success	64%	72%	73%	71%
TB abandon	7%	7%	5%	10%

Conclusion: Introduction of successful HIV care did not hinder TB outcomes. The reasons for steady case detection and improved treatment results are discussed.

PS-100806-14   Roll-out of TB-HIV activities in Kivu North, DRC. Major outcomes and lessons drawn

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Introduction: Since 2005, the Integrated HIV Care/UNION (IHC) project was implemented in 2 DR Congo provinces in order to promote one stop approach of care among TB-HIV co infected patients. IHC project started in 13 TB clinics in Kivu North. During 2009, new collaborative TB-HIV activities were being rolled out in 10 TB clinics throughout Kivu North. Currently integrated TB-HIV services cover 33% of TB clinics in the North Kivu province.
Objectives: To evaluate outcomes after the rolling-out TB-HIV activities from 13 TB clinics to 23 in North Kivu and to draw lessons for future scaling-up.
Methods: We did a retrospective review of all records reported by the provincial TB coordination (CPLT) in 2009. From cases notification gathered in TB registers, we determine the major outcomes/indicators of the implementation of TB-HIV activities in Kivu North.
Results: In 2009, a total of 2555 TB patients did get access to VCT services in 23 TB clinics in Kivu North. Preliminary data shows that 81% (2070) have been tested for HIV. Overall 19% (402) of TB patients, who were tested, are found to be HIV positive. Of 402 co-infected patients, 65% (263) got access to cotrimoxazole prevention and 26% (106) to ARV treatment.
Conclusion: Kivu North IHC project has boosted the implementation of TB-HIV activities however services coverage is still limited due to the lack of adequate provisions of supply and funds. IHC project model should be used for rolling-out TB-HIV activities in the entire country.

PS-100822-14   ART retention at 6 months and 12 months in a TB-HIV collaborative project at Mabvuku Polyclinic, Harare, Zimbabwe

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Introduction: In September 2008, City Health Department, in collaboration with the Union, started a pilot program to test the feasibility of integrating HIV care including antiretroviral treatment (ART) among TB patients. Services offered at the site include Provider Initiated Testing and Counselling (PITC),

Cotrimaxazole Prophylaxis, TB investigations and TB Treatment including partners.

Aim: To determine the ART retention rates of TB coinfected patients.

Objective: To assess the possible outcomes of patients on ART at 6 months and at 12 months.

Methodology: A descriptive desk study was done. Records of the participants who visited Mabvuku Polyclinic in Harare for Integrated HIV Care services from September 2008 to September 2009 were retrieved and reviewed. Information was extracted from TB and ART registers. Data was analysed manually.

Preliminary Results: 232 TB coinfected patients were on the ART register for at least 6 months. Eighty-two percent of the patients were alive and still receiving ART. Seven percent of the patients died and ten percent were lost to follow up. Outcome analysis at 12 months was done for 97 patients. Seventy six percent were alive, 12% dead and 1% transfer out.

Conclusion: The ART retention rate is good both at 6 and 12 months. How ever there is need to strengthen follow up services and adherence counselling.

PS-100847-14   Lack of adequate TB-HIV activities financing in the DR Congo

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Introduction: To meet the Millennium Development Goals (MDGs) the NTP DR Congo has developed its strategic plan 2006–2015, whose total cost is estimated at US$545 861 563. The TB-HIV activities account for US$135 978 235 or 25% of the total budget. However currently the service coverage of TB-HIV co-infection remains insufficient across the country.

Aim: This study aims to evaluate the implementation of TB-HIV activities in the light of available funding.

Methods: A retrospective review of financial reports of the NTP DR Congo from 2006 to 2009 did help to account the financing of HIV-TB co-infection and to analyze progress reports coming from provincial TB coordination in order to estimate the coverage of TB-HIV activities within the country.

Results: The analysis shows that 37% of available funding is coming from the Global Fund, 62% from traditional partners and 1% from bilateral cooperation. From 2006 to 2009, the NTP has mobilized for the implementation of activities co-infection TB-HIV a total of 4 117 457 US on US$23 362 188, which means only 18% of expected funds. It appears that only 20% of TB patients know their HIV status.

Conclusion: The mobilized resources are insufficient. A gap of 82% over the funding continues to limit the expansion of TB and HIV activities coverage. To meet the MDGs in lane to fight the TB-HIV co-infection, DR Congo should accelerate funds mobilization.

PS-100910-14   Good practices of HRD and management policies for TB-HIV programmes

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Background: NACP Pakistan recently get approval of PC-I (Project Cost-I) for worth Rs.1930.603 million for 5 years for implementation of HIV-TB activities of National Control Programmes.

Methods: NACP Pakistan is mixture of Government, WHO, Global Fund Round-9 and several NGO employees working under one Umbrella of NACP and supervision of National Manager. Ministry of Health is authority of approvals, instructions and monitoring all activities for TB-HIV Co-infection disease.

Key findings: NACP Pakistan has implemented HIV-TB Treatment program all over Pakistan. Expansion and development of comprehensive strategy for Quality assured sputum smear microscopies are main challenges but implementation of HR HRD & M is one of key challenge we need to actually trained and retain employees. Justified remuneration system, performance based appraisal for increments/increases, retain trained staff specially service provider like Lab Technicians.

Conclusion: Professional hiring and retaining trained staff and justified professional trainings, performance based (Pay for performance) increase/enhance will boost the output/moral of an employee. In experience Microscopist/Lab Technician increases their performance by providing professional trainings, motivation and incentive. Continuation of Performance appraisal and pay for performance system need to start.

PS-100919-14   Global Fund support to address TB-HIV co-infection and multidrug-resistant TB

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Background: Increasing rates of TB-HIV co-infection and multidrug-resistant tuberculosis (MDR-TB), have led some countries to include both activities in their proposals to the Global Fund to Fight AIDS, Tuberculosis and Malaria. This study demonstrates how the Global Fund has addressed the critical issues of TB-HIV co-infection and MDR-TB, by scaling up funds for high-burden countries and recommending countries to address them.

Methods: The funding approved by the Global Fund, from 2002 to August 2009, was analyzed using a TB subaccount framework to assess the proportion of funds aimed at TB-HIV and MDR-TB. Information on TB burden was obtained from WHO global TB control reports.

Results: The Global Fund approved US$2.5 billion for TB control programs in 110 countries, of which

67% went to the WHO-defined 22 high-burden countries and more than 50% went to the WHO-defined 27 countries with high MDR-TB levels. The Global Fund approved US$384 million for TB-HIV programs in the study period. The scale-up in sub-Saharan Africa was greatest as was the largest share of funds (65%). The region accounts for the highest TB-HIV burden (80%). The Global Fund invested about 19% of cumulative funding for TB-HIV control in South-East Asia, the region accounting for 15% of the global TB-HIV burden.

The Global Fund has scaled up funding for TB control by 95% in Central and Eastern Europe and Central Asia since 2006 to meet increasing MDR-TB rates in this region. Out of 27 high-burden MDR-TB countries, 15 are located in this region and 10 countries are funded by the Global Fund. MDR-TB funds largely finance implementation of DOTS as well as essential TB medicines.

Conclusions: By approving and scaling up funds aimed at fighting TB-HIV and MDR-TB, the Global Fund and partners play a major role in helping countries attain the Stop TB partnerships global targets for 2015, of reducing the global burden of TB-HIV and halving prevalence and death rates from the 1990 baseline.

PS-100965-14　TB-HIV collaboration in Ukraine: results and challenges

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Background: TB-HIV incidence and mortality increased 2.5 times from 2004 till 2008.
Aim: To determine challenges in the implementation of WHO Policy for Collaborative TB-HIV activities in three regions of Ukraine with total population of 8 million.
Methods: An assessment of TB-HIV collaborative activities and retrospective analysis of TB mortality in patients 15 years and older was performed by regional experts using a tool based on WHO recommended indicators.
Findings: Although coordination bodies on TB and HIV/AIDS exist in all regions, only one of three regions has a joint TB-HIV plan and routine monitoring activities. No funds are allocated specifically for TB-HIV activities in any of the regions. Number of governmental and non-governmental institutions involved in TB and TB-HIV activities varies from 4–10 between regions, out of which only few represent HIV communities and none TB communities.
Of 2762 TB death cases from three regions included in the study, HIV voluntary counselling and testing was provided to 58–86% (depending on region). Average HIV prevalence in 1681 deceased TB patients with known HIV status was 44.4%. Provision of antiretroviral treatment (ART) for TB-HIV co-infected patients in regions was low—14 (1.98%), 2 (1.56%) and 5 (10.64%) patients.
Conclusions: Coordination between TB and HIV programmes is insufficient and need considerable improvement. Taking into consideration that average coverage of ART for HIV infected patients in Ukraine is 35%, access of TB-HIV co-infected patients to HIV services is significantly limited. Lack of community involvement is obvious in all regions.
Recommendations: Promoting TB-HIV co-infection issues with health authorities at all levels should be continuously performed. Normative documents on TB-HIV should be revised; TB-HIV coordination algorithms elaborated and implemented. Community involvement as important stakeholders in TB-HIV issues should be increased.

PS-101201-14　Participation of different health sectors in notification of tuberculosis into the national control program

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Objective: To determine the role of health sectors in diagnosis/referring PTB suspect and or patient for management under the care of National TB control Programme.
Design: A prospective study.
Setting: Respiratory and Chest Disease Institute; Baghdad, from 1st Jan–30th Jun 2006.
Methodology: Among 11 152 attendants (TB suspect), seeking medical care, 729 patients confirmed as new PTB,464 as SS+ and 265 as SS− PTB and most (80%) are in reproductive age group, with male to female ratio of 1.5:1. Among 585 PTB patient inquired, 252 patient (43%) referred from private sector and 117 (20%) from public Hospital, while only 19 (3%) from primary Health care centers (PHCC) in which DOTS services were adopted.
Discussion and conclusion: The study revealed that the main referral source of PTB suspect and or patients to the Institute (National TB Control Programme) is the Private sector, while in the contrary PHCCs play minor role in this referral. This indicates that many patients may remain without registration in the National Control Programme. Lack of involvement of different National Health sectors in TB control activities is the leading cause for poor case detection and notification by National Programme. Using Public-Private Mix (PPM) approach will improve referral routines and information exchange between public and private providers which in turn can help to improve general health information systems.

PS-101281-14 Impacto del plan de acción para disminuir la tuberculosis en personas que viven con VIH o diabetes e TB-VIH

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Antecedentes: En México, el porcentaje de personas coinfectadas con VIH y MTb varia entre 4% y 12% en los últimos 26 años. Durante este periodo de 12,629 registros de TB-SIDA, viven actualmente 3.800 (30%), La diabetes y la obesidad van en aumento en el país y su comorbilidad con la tuberculosis oscila entre 20% y 27%, por lo que México ha puntualizado la coordinación con ínterprogramática la realización de actividades operacionales diversas.
Objetivo: Describir las tendencias de las comorbilidades y la tuberculosis TB-VIH/SIDA-DM y el impacto de las acciones integrales de salud en El País.
Metodología: Implementación de 12 líneas de colaboración interprogramática recomendadas por OPS/OMS, y 14 líneas de acción para la coinfección TB/DM, con búsqueda de sintomáticos respiratorios entre personas con VIH-glucosa o con SIDA > 180 mg/dl y contactos con casos de TB activa, una capacitación personas Afectadas En colaboración con las ONGs y activistas y capacitación a médicos, enfermeras que Líderes de las Naciones Unidas y ATIENDEN personas con VIH o DM.
Resultados: La tendencia de la coinfección TB-SIDA es ascendente, la colaboración interprogramática Se han mejorado con el sistema de información y la sistematización de acciones de detección y tratamiento de la tuberculosis, en 2009 el 66% de casos de tuberculosis coinfectados hijo de SIDA de forma pulmonar, miliar 11,4%, 5,2% ganglionar meníngea 11,4% y 6% en formas mixtas. La comorbilidad con DM fue de 18,2% con 3.210 casos.
Conclusiones: La Coordinación interprogramática TB/TB y SIDA/DM, es clave para mejorar calidad de vida de las personas con VIH-SIDA o DM y sistematizar de las pruebas de VIH en enfermos de TB y oferta de pruebas de TB y quimioprofilaxis para personas con VIH o DM.

PS-101372-14 Improvement of combatting co-infection TB-HIV by collaboration between the NPLS and NTP, Kinshasa, RDC

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Framework: Faced with the collaboration remained still in intentions between the two programs NPLS and NTP, an Italian NGO CESVI has initiated a project including two teams in a multi-hospital involved in the fight against co-infection TB-HIV in the hospital.

Objective: Evaluate the results obtained by the hospital that involved both NTP and NPLS programs.
Method: Comparative study of results obtained by 2 hospitals, one of which involved collaboration between NPLS and NTP and the other without collaboration.
Results: A year after the launch of this project: 11 supervisions joint, 4 meetings, setting up two gateways for co-infection hospital collaboration with NPLS and NTP cons no joint supervision, no meeting and only 1 door VCT. 180 registered cases of TB, 180 with counseling, 108 tested, 13 co-infected for co-infection hospital collaboration with NPLS and NTP against 62 registered cases of TB, 52 with counseling, 17 tested, 0 cases co-infected, 463 PVV including 250 eligible and 154 put under ARV treatment, 168 submitted to Ziehl including 12 co-infected for co-infection hospital collaboration with NPLS and NTP cons no data on hospital with collaboration.
Conclusion: The structured cooperation between the two programs NPLS and NTP improves the care of cases co-infection TB-HIV.

PS-101383-14 Integration of TB-HIV co-infection into primary health care: a pilot project, Kinshasa

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Framework: Having regard to the AIDS pandemic having an impact on tuberculosis, a working group TB-HIV has been put in place in Kinshasa in 1999 and a pilot project was started in 2004.
Purpose: To assess the effectiveness of the integration of TB-HIV co-infection into the PHC depending on the functionality of the area of health.
Method: Comparative study of results obtained by two areas of health involved in this project after five years of its launch. Choice of a zone of health less functional and other functional to PHC.
Results: Cases of TB registered: 799 cases to 393 for zone of health less functional against 1.492 case 1617 case for the functional to PHC, Cases counseling for test: 361 to 365 for the first with 1% increase against 450 to 1300 for the second with 277% increase, Cases having accepted the test: 345 to 357 for the first with 3% increase against 435 to 1.092 for the second or 217% increase, Case co-infected: 133 to 40 for first and 129 to 172 for the second.
Conclusion: Effective integration of the fight against co-infection TB-HIV in the minimum packages the zone of health must take account of the degree of functionality.

PS-100350-14 Investigación operativa fuente de evidencia para decisiones en gestión de suministros TB y VIH en RD

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Introducción: En 2006 los programas de TB y VIH enfrentaban problemas en el suministro de medicamentos y métodos diagnósticos. Con recursos de USAID/RD, MSH realizó investigaciones operativas para fundamentar la implementación de acciones correctivas basadas en evidencia.

Intervención: Un estudio de costos de mono-fármacos y combinaciones a dosis fijas (CDF) para TB, justificó la compra de CDF al Global Drug Facility (GDF) en 2007. Otro sobre su impacto en el abandono, consolidó la extensión de esta intervención a todo el país. Un estudio del suministro de insumos diagnósticos respaldó la implementación de guías estandarizadas y la adquisición de kits de baciloscopia al GDF en 2009. En 2009 y 2010, investigaciones de la situación del suministro en el Ministerio de Salud (MS) evidenciaron desabastecimiento de medicamentos y recursos diagnósticos, particularmente de VIH.

Resultados: RD fue el primer país de América Latina en adquirir CDF y kits de diagnóstico al GDF. En 2009 todos los laboratorios (156) seguían procedimientos operativos estandarizados y contaban con kits. Desde 2007 todos los pacientes con TB son tratados con CDF. Un estudio realizado en 2009 demostró que esto redujo el abandono en 5%. Ambas intervenciones ahorran al país cerca de USD 1 millón por año. La solución eficiente y sostenible a los problemas de suministro del Ministerio de salud es la implementación de un sistema único, decisión que fue adoptada por las autoridades de salud sobre la base de estas investigaciones.

Conclusiones y recomendaciones: Información basada en evidencia a través de Investigaciones operativas, trasladadas a argumentos políticos, permiten la introducción de tecnologías y buenas prácticas en salud pública. Esto logros son posibles si se alcanza coincidencia de intereses entre autoridades de salud, técnicos nacionales y agencias de cooperación.

PS-100359-14 Areas of vulnerability to HIV-TB co-infection in Ribeirão Preto, São Paulo, Brazil, 2006

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Objective: To identify areas of vulnerability for HIV-TB co-infection in Ribeirão Preto, São Paulo, by analyzing the spatial distribution of cases reported in 2006.

Methods: This is a descriptive ecological study. The study population consisted of co-infection cases reported as new and involving individuals living in Ribeirão Preto. Individual and collective variables were selected respectively from the TB-WEB information system and from the year 2000 demographic census. New cases were georeferenced based on the addresses obtained from the TB-WEB and ArcGIS 9.1 software. The analysis unit was the census tract and the statistical analysis was that of main components. After determining the explicative factors, one factor was chosen as the responsible for the greatest part of the total variation (83%) and was referred to as the socioeconomic factor. The sectors were ordered from larger to smaller and divided according to terciles, resulting in three socioeconomic groups: superior (best conditions), intermediate and low (worst conditions). Incidences were calculated according to the referred grouped sectors.

Results: 48 new cases were considered. Patients were mostly (68.7%) men, were aged between 20 and 39 years (47.9%), had secondary level education (58.3%) and had pulmonary TB (75%). The area corresponding to the lower socioeconomic group presented the highest HIV-TB incidence (11.5/100 000 population), followed by the intermediate (8.3/100 000) and superior (4.8/100 000). This shows that there is a relationship between low socioeconomic levels and the occurrence of TB among individuals with AIDS.

Conclusion: The analysis permitted to identify areas of vulnerability for HIV-TB co-infection and will allow for developing more effective actions and achieving more satisfactory outcomes in controlling these diseases, thus favoring a better distribution of human and financial resources.

LABORATORY SYSTEMS AND QUALITY ASSURANCE

PS-100108-14   TB culture and DST proficiency testing in 2009–2010 in the Russian Federation

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TB laboratory assays proficiency testing (PT) had been regularly performed in Russia since 2001. In 2009, 160 laboratories had participated in the 1st line DST PT on Löwenstein-Jensen media. Additionally 17 laboratories had participated in PT of the TB mycobacteria culturing, identification and DST using liquid media. In 2010, 132 laboratories will participate in 1st and 2d line DST and 31 laboratories—in culture and DST in liquid media. The 2009 DST panel consisted of 20 *M. tuberculosis* cultures susceptible and resistant to 1st line drugs. 160 laboratories had participated, 33 laboratories had provided 100% efficiency for all 1st line drugs, 26 more—to Isoniazid (INH) and Rifampicin (RMP) only. 59 laboratories demonstrated less than 90% efficiency either for INH or RMP. In 2010 the panel will be comprised of the strains provided by the Sweden Supranational laboratory, susceptible and resistant to 1st and 2d line drugs. The panel for liquid media culture and DST assays in 2009 consisted of 10 samples which were *M. tuberculosis* samples susceptible and resistant to the 1st line drugs and Pyrazinamide. Some of the strains were deliberately contaminated by E. coli. 89% of all samples were correctly identified as *M. tuberculosis* by participants. Average sensitivity was 100% for INH, RMP and Streptomycin and 80% and 96% for Ethamabutol and Pyrazinamide, correspondingly. Average specificity was 97–100% for all drugs.

PS-101003-14   Development of external quality control programme through the digital photography of culture in laboratories

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Background: In Bolivia the bacteriological method are implement in all the regions,there are 509 laboratories they make direct smear examinations, and the activities of all of them are complement with culture method, 17 laboratories establish in seven regions, they are doing culture in solid medium Löwenstein-Jensen, Stonebrink and Ogawa medium.The number of the cultures in the year is around 5.500 to pulmonary tuberculosis and 689 for extrapulmonar tuberculosis. The quality assurance is implement in direct smear examinations, and culture method, and the external quality control in culture many times were difficult to do, sometimes the culture samples is not easy to send some laboratories, the transport system is not always available, also the tubes with culture positives, sometimes the tubes arrive spoiled, and the conditions of the transport of the tubes are not good according with the international regulations.
Method: Our challenge was, to improve the program of the external quality control, and in the National reference Laboratory we prepare a panel with 30 photographs of *Mycobacterium tuberculosis* cultures, with disgonic and eugonic grow, the observation of each bacteriologist was done in two ways: through internet, all of the bacteriologist to can to review the photography's at the same time, same day, and the same test was apply during the direct supervision, the concordance of the interpretation was of 94% in the positives culture $(+,++,+++)$ the discordance was 6% in disgonic grow tubes.
Conclusions: Is very useful to apply this kind of method, there are not risk of contaminations in the laboratories, in human recourses and also in the environment.

PS-100767-14   Improved bacteriological coverage and HIV-TB integrated care through use of lay workers

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Background: South Africa (SA) has one of the highest TB and TB-HIV co-infected burdens globally and one of the worst TB treatment programmes, resulting in high TB mortality and rising rates of DTB. In the hospital setting, programmatic weaknesses and staff shortage contribute to poor implementation of TB guidelines and poor outcomes.
Aims: To assess use of an inpatient TB support service ('TB Warriors'), consisting of specially trained lay persons.
Methods: In June 2006, a 'TB Warrior' service consisting of 2 lay persons, was introduced at Edendale Hospital. Doctors were provided with 'suspect rounding forms' to list TB suspects and a central location for depositing filled forms. 'Warriors' went bedside to all listed suspects, provided sputum specimen cups, checked and completed the doctor's sputum request form, hand carried specimens to the lab, collected lab results and returned them to the ward and notify doctors of positive results. Warriors also provided HIV testing & counseling, TB education and instructions on transfer to their local clinic.
Results: From May 2006 to Feb 2010, over 6660 TB suspects were supported by the 'TB Warrior' service,

which represents ~25% of suspects admitted during this period. Bacteriologic coverage increased from 13% to 100% for warrior supported suspects, but remained 0% for those not seen by the warriors. HIV counseling and testing increased from irregular/rare to 100%, with immediate referral for ART. All warrior supported patients received standardized education about TB and instructions on transfer to their local clinic.

Conclusion: In resource-constrained settings with high TB burden, use of specially trained lay workers, may improve TB services and outcomes. Empowering fewer individuals, to assume responsibility for more of the steps in the chain of TB services, may result in more successful and cost-effective TB programme implementation.

PS-101007-14   Trends of MDR-TB at the reference laboratory in Bolivia

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Introduction: In Bolivia the Laboratory Network established standard procedures to diagnosis of tuberculosis disease, in bacteriological method direct smear examinations, culture, identification test and drug sensitivity test. The direct smear examination, all the laboratories are doing Ziehl-Neelsen method, the culture in solid medium Löwenstein-Jensen, Stonebrink, and Ogawa medium, and drug susceptibility testing (DST) according the proportional method. All the positive cultures are sent to National Reference Laboratory, with the epidemiological information, the number of cultures was increase from 2006 to 2009, and the identification of MDR-TB patients were done trough the results of DST, for these purpose our laboratory receive the external quality control of supranational laboratory of our region.

Method: We analyzed the results in the record of National reference laboratory of all the DST of last 7 years, to compare the number of MDR-TB patients.

Results: From 2003 to 2009 the number of cultures in Bolivia to increase 3053 in 2003 to 5615 (54%) in 2009, in all the positive cultures from the regions are send at the National reference Laboratory performed DST, and the MDR-TB we identify: as follows: 49 (15%) of 324 cultures in 2003, 80 (25%) in 325 in 2004, 76 (7%) in 2005: 44 (11%) in 400 in 2006, 28 (8.2%) in 347 in 2007, 42 (4.9%) in 355 and 101 (11.9%) in 669 in 2009.

Conclusions: The total number of MDR-TB patients, in Bolivia is 420 from 2003, to 2009, they represent the 15% of total positive cultures , and the MDR-TB increase from 2003: 49 MDR-TB cases, and 101 MDR cases in 2009, the surveillance improve according the number of cultures performed in the Laboratory Culture Network.

PS-100388-14   External quality assurance for drug susceptibility testing in laboratory of Donetsk TB hospital

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Setting: MDR-TB project on diagnostics and treatment of MDR-TB patients started in Donetsk oblast in 2006 with the support of local charitable foundation 'Development of Ukraine'. Drug resistance surveillance (DRS) preceded it. In order to conduct DRS in Donetsk oblast, Ukraine, the trilateral agreement on external quality assurance (EQA) for drug susceptibility tests (DST) between Donetsk oblast health administration, Donetsk oblast TB hospital and supranational bacteriological laboratory in Gauting, Germany, was concluded in 2005.

Aim: As reliability of DST results is crucial for diagnostics of MDR-TB, the aim of this research was to assess results of EQA for DST to first-line TB drugs that are performed in bacteriological laboratory of Donetsk oblast TB hospital.

Methods: Panel testing using culture samples received from Germany was applied; besides samples with bacteriological material were sent to Germany during DRS for rechecking.

Results: During 5 years of collaboration with supranational laboratory, panels were received from Germany twice and samples were sent to Germany also twice for EQA purposes. The last 5th panel from Germany was received in February and is processed now. The results of EQA are presented in the Table.

Table   Coincidences of DST results

	1 circle 2005	2 circle 2006	3 circle 2007	4 circle 2008
Isoniazid	90%	100%	95%	100%
Rifampicin	95%	75%	100%	100%
Ethambutol	95%	75%	70%	90%
Streptomycin	85%	80%	93%	100%

Conclusion: Five-year collaboration with supranational laboratory on EQA for DST to 1st line TB drugs allowed improving quality of the bacteriological tests that influenced positively to reliability of laboratory diagnostics of MDR-TB.

PS-100684-14 Situational analysis of tuberculosis diagnostic primary health centre laboratories in Zambia

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Background and challenges: Improved performance of laboratory facilities for *Mycobacterium tuberculosis* diagnosis have provided for early disease identification and treatment. Health centre level diagnostic laboratory facilities in Zambia are, however, faced with challenges that include inadequate staff, limitation of laboratory diagnostics for smear microscopy, inadequate standard operating procedure manuals and other reporting tools.
Intervention: A situational analysis of 88 primary health centre level laboratories was done in five provinces in Zambia using a standard, structured checklist and review of laboratory registers. Staff qualifications, documentation, availability of standard operating procedures, staff workload, smear positivity rate, equipment, supplies, and disposal systems were assessed.
Results and lessons learnt: There were 72 qualified laboratory staff present during the assessment, 30 of the 72 were medical technologists and 42 were laboratory technicians. 27 of the 72 had received training in external quality assessment (EQA) and 41 of the 72 had received training in Acid Fast Bacilli (AFB) smear microscopy. From the 88 laboratories, the average sputum positivity rate was 12.5% and the annual workload was 512. 37 diagnostic centers had standard operating procedures and 37 of the laboratories assessed were using National Tuberculosis Program (NTP) approved laboratory request forms. 49 had weigh balances and 34 had water distillers. Some laboratory consumables were in short supply. The main methods employed for disposal of laboratory waste were burning and incineration.
Conclusions and key recommendations: Financial and technical support of laboratories from national to primary health care level must be a priority. Prevailing laboratory networks require establishment of adequate, well trained and motivated staff, provision of national reporting and recording tools, standard operating procedures, laboratory equipment and supplies.

PS-101361-14 Use of containerized laboratories in the ZAMSTAR TB Prevalence Survey in Zambia: a progress report

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Background: ZamLab CTL containerized BSL3 TB laboratories were designed, constructed and deployed to four existing health facilities in Zambia for use in the ZAMSTAR TB Prevalence Survey. From December 2009 to January 2011, the survey will test 80 000 people from 16 sites in Zambia for active *M. tuberculosis* infection. Laboratories are staffed by biomedical scientists, newly-hired or from the hosting institutions, who have successfully completed an intensive training course in mycobacteriology and BSL3 practices. Upon completion of the ZAMSTAR survey, the laboratories will be turned over to the Zambian Ministry of Health for use in a national TB prevalence survey and to expand the availability of TB diagnostic services.
Methods: Each ZamLab CTL processes up to 100 sputum specimens per day for TB culture using the manual MGIT liquid culture system. Cultures are prepared in duplicate and scanned for growth once per week using the micro MGIT fluorescent reader. Supernatants from fluorescence-positive cultures are stained with Ziehl-Neelsen to confirm the presence of AFB by microscopy, then tested using the BD MGIT TBc Identification test to confirm the presence of *M. tuberculosis* complex. Fluorescence-positive/*M. tuberculosis*-negative cultures are categorized as 'non-tuberculous mycobacteria (NTM) or bacterial contamination' pending identification of the contaminant.
Results: As of March 2010, the laboratories had processed 5857 sputum samples and inoculated 11 714 duplicate MGIT cultures. Of the 11 714 duplicate MGIT cultures, 263 (2.2%) were fluorescence-positive/*M. tuberculosis* complex-positive and 1449 (12.4%) were fluorescence-positive/*M. tuberculosis* complex-negative.
Discussion: Containerized BSL3 laboratories appear to be a useful tool for performing a large-scale TB prevalence survey in Zambia. Training and supervision of staff, monitoring of culture contamination rates, and maintenance of facilities and equipment are of critical importance in a resource-limited setting.

PS-100816-14 External quality assessment system in TB control programme of Bangladesh

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Background: BRAC, an NGO, implementing TB control program covering 89.5 million populations in Bangladesh. In collaboration with national TB control program. National guideline of EQA is based on blinded recheck system for laboratory performance and quality control.

Objectives: To ensure quality of AFB microscopy at microscopy center level through providing EQA services.

Interventions: A total of 21 EQA laboratories have been established to check the quality of 678 microscopy center at BRAC supported area. Monthly 5 slides collected randomly from each microscopy center and rechecked by first controller at EQA level to assess the quality. Regular feedback is provided subsequently from EQA to microscopy center that help to develop technical competency of laboratory staff. If any slide is discordant at EQA laboratory then it is further evaluated by second controller at center level. The first controllers visit routinely each microscopy center quarterly to monitor laboratory quality which includes reagent, smear microscopy.

Result: From January to September 2009, 2.07 million slides were examined for diagnosis and follow up at BRAC supported area of which 28 934 slides were rechecked. Among them 0.47% slides (Total = 136, HFP = 5, HFN = 106, SFP = 1 & SFN = 24) were found discordant up to September 2009, which was previously 0.67%, 0.61%, 1% and 2% in 2008, 2007, 2006 and 2005 respectively.

Conclusion: EQA system helps to improve the quality of laboratory activities, including quality of smear. Corrective measures taken following the feedback are helpful for programme performance.

PS-101210-14 Evaluation of internal quality assessment on DSSM of the National Reference Laboratory, Philippines

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Setting: National Tuberculosis Reference Laboratory, Philippines.

Background: Since the establishment of the National Tuberculosis Reference Laboratory in 2002, internal QA of smeared slides has been done to maintain the skills and proficiency of the laboratory staff in Direct Sputum Smear Microscopy (DSSM). It is important to have competency in TB Microscopy, for NTRL is mandated to conduct training on DSSM and QA, and monitor laboratory activities in the network.

Objective: To evaluate the competency of NTRL staff in DSSM using the internal QA results in slide reading and smear preparation.

Method: Specimens previously processed in DSSM were collected weekly from the microscopy centers near NTRL. Each specimen was again smeared, stained and read by each NTRL staff. The lab. supervisor quarterly collects and selects slide using LQAS for validation. The senior med. tech. blindly rechecked the slide reading and assessed smears using the six checkpoints on quality smear preparation. Over-all agreement and number of Major Errors (HFP & HFN) and Minor (Quantification) Errors were used as indicators in slide reading evaluation, while at least 90% good quality in each check points was used in smear assessment.

Result: For the past five years, the over-all agreement is consistently high ranging from 95% to 98.50%, indicating good performance in the smear slide reading. While in the six checkpoints, only specimen quality does not reached the 90% target rate. This is because the most specimens collected were already liquefied. The other checkpoints (staining, cleanness, thickness, size and evenness) ranging from 92% to 100%.
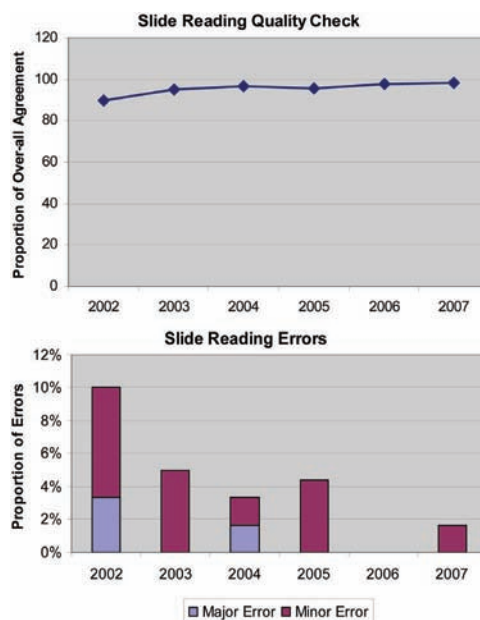
Conclusion: Internal Quality Assessment of smeared slides is indeed helpful in maintaining skills and proficiency in TB Microscopy. This also serves as indicator of lab. staff performance, especially for those NRL that are not yet assessed by a supranational laboratory.

PS-101354-14   Scale-up of tuberculosis laboratory services in Serbia

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Over the past five years the National Tuberculosis (TB) Control Program in Serbia supported by Global Fund grant developed the strategy for the strengthening of existing laboratory services. The strategy included the following: acquisition of appropriate equipment, standardization of laboratory procedures, implementation of quality assurance programs for microscopy and drug susceptibility testing (DST), improvements in recording and reporting system, and training activities. The TB laboratory network currently comprises 35 laboratories, out of which 3 perform microscopy only, 25 perform microscopy and culture, and 7 laboratories perform microscopy, culture and DST (one of them is National Reference Laboratory, NRL). High quality microscopes have been procured for all laboratories included in the network, while biological safety cabinets have been procured for 25 laboratories. An automated liquid media system and molecular line probe assays for rapid identification of mycobacterial cultures and detection of MDR *Mycobacterium tuberculosis* strains were introduced. All laboratory procedures have been standardized in accordance with newly published national guidelines for microbiological diagnostics of TB. NRL under supervision of Supranational Reference Laboratory in Borstel, Germany conducts external quality assurance programs for smear microscopy and DST. Another significant improvement is introduction of computerized system for data collection in 28 laboratories. The strategy for laboratories strengthening contributed to improved efficiency and reliability of TB laboratory services in Serbia as indicated by increase in rate of culture confirmed TB cases from 52% in 2005 to 81% in 2009. Future efforts will be focused on expanded application of rapid TB diagnostics and continuous education of laboratory personnel.

PS-101168-14   Challenges in biosafety level 3 tuberculosis laboratories in Nigeria

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Background: Biosafety level (BSL) 3 laboratories are recommended for handling specimen processing, culture inoculations/reading, highly concentrated cultures for indirect susceptibility testing and species identification. The high burdens of HIV and TB have together created additional complication in which the capacity of health care infrastructure is a deciding element in Nigeria. Biosafety level 3 laboratory require high technology equipment with controlled ventilation that maintains directional airflow.

Challenges:
- Inadequate monitoring of bio-containment laboratory design and equipment by qualified personnel
- Implementation of TB culture is uneven; observation of safety regulations by designated safety officers most of whom are yet to be trained on biosafety and bio-containment is lacking
- Equipment upkeep, maintenance and constant supplies of necessary materials is a great challenge due to inadequate qualified local maintenance and procurement officers
- The systems lack constant and regular audits monitoring by qualified auditors to ensure implementation of systems are up to date and working
- Few qualified and dedicated staffs are availability to handle the high technology structure and infrastructures
- Inadequate staff strength to address existing workload which was compounded by staff attrition

Recommendations and conclusion:
- Need for training for facility staff
- Safety precautions and regulations required for BSL3 laboratory operations need constant monitoring by qualified safety
- Regular maintenance of equipment and supplies
- Constant monitoring of quality management systems with regular audits by qualified auditors
- Hire adequate dedicated and qualified staffs needs to ensure quality work performance
- The turnaround time for effective patient management results must be achieved
- Address laboratory staff attrition by paying advocacy visits to go

PS-101083-14   Strengthening laboratory practices towards accreditation in Nigeria

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Background: In Nigeria, three laboratories desirous of implementing Quality Management System (QMS) in acquiring accreditation status were strengthened to work towards practice in accordance with accepted norms of accreditation and certification using the ISO 15189 for Medical Laboratories. Two of the laboratories located at Zaria (serves population of >40 million people) and Calabar (serves population of about 12 million people) are high containment levels. The third laboratory is a Biosafety Level 2 facility serves population of >50 million people.
Intervention: The ISO15189 standard fifteen management and eight technical requirements necessary

for accreditation were considered. The WHO /AFRO intermediate checklist was the major tool being used for measuring compliance to the ISO15189.

Results and lessons learnt: All Technical SOPs completed and controlled according to ISO15189. 34 facility staffs trained on technical procedures for TB/MDR-TB culture and DST procedures including MTBDRplus line probe assays. Draft of Quality Policy, Quality and Safety Manuals were developed. Using BSL3 safe work practices. Equipment listing for all facilities was documented. Standard Operating Procedures for preventive maintenance were developed. Some quality parameters such as EQA for Hain assay, PT for smear microscopy and control strains for culture already being monitored. All staffs were sensitized on the benefits of QMS. The issue of continuous supply of electricity was a great challenge.

Conclusion and key recommendations:

- The progress by all 3 laboratories has been phenomenal
- Supervisors and Managers need to encourage and supervise progress to ensure that all staff are involved in this progress
- Need for periodic audits from external agencies to monitor progress and provide feedback
- Address issues on intermittent power supply through provision of battery

PS-101092-14   Improving tuberculosis diagnostic capacity among local laboratories in a rural setting

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Background: The TB vaccine preparation project which started in 2008 is being implemented in Iganga/Mayuge Demographic Surveillance Site (DSS), a rural setting in Eastern Uganda. As part of building capacity for future TB vaccine trials, the study collaborated with the National Tuberculosis and Leprosy Program (NTLP) to strengthen TB diagnostic capacity in local laboratories within the site.

Objective: To build local capacity to improve TB smear microscopy.

Method: At commencement, the project identified gaps in TB microscopy knowledge and technical skills, non-functional equipment, frequent supplies stockout and poor infrastructure as foremost needs among the local laboratories. The project intervened by providing functional equipments, renovating 7 local laboratories, buffering up laboratory supplies, training

and support supervising laboratory staff. In collaboration with District Laboratory Supervisors, the project ensured all laboratories participated in quarterly external quality assessment (EQA) blinded rechecking with NTLP Laboratory.

Results: Currently, 12 laboratories in the DSS including privately-owned are now participating in EQA; an increase from 5 before this project. Preliminary EQA data analysis shows ongoing improvement in TB smear microscopy, reduction in major and minor errors over time from 54 smears rechecked in 2007 with specificity = 1, sensitivity = 0.85 to 299 smears rechecked in 2008 with specificity = 0.98, sensitivity = 0.94 and 169 smears rechecked in 2009 with specificity = 0.97, sensitivity = 0.90.

Conclusion: Preliminary EQA results obtained during this intervention show it is feasible to establish quality assured TB diagnostic capacity for local laboratories within TB vaccine trial sites in collaboration with NTLP through providing appropriate infrastructure upgrade, additional technical skills and buffering up laboratory supplies.

PS-100140-14   Improving the laboratory diagnosis of TB through proficiency testing in Northern Uganda

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Background and challenges to implementation: In low-income countries with high tuberculosis (TB) prevalence, sputum smear microscopy using the Ziehl-Neelsen (ZN) technique remains the most cost-effective tool for diagnosing patients with infectious tuberculosis. Maintaining a high standard of sputum smear microscopy technique is an indispensable component to attaining an effective TB control programme. Northern Uganda Malaria AIDS Tuberculosis Program (NUMAT) is a USAID-funded program working in 9 post conflict districts that supports laboratory services through building capacities of laboratory personnel among others.

Intervention or response: NUMAT contracted supervisors from Ministry of Health to conduct quarterly technical support supervision in all laboratory units the program assists within the nine districts. So far, five supervision rounds were conducted in the last 18 months. When supervision visits are conducted, proficiency tests are performed and results assessed on the spot. Immediate feedback is also given to lab personnel.

Results and lessons learnt: From July 2008 to December 2009, the number of participating lab units increased from 36 to 68, with additional lower level facilities being included in the exercise. The proportion of proficiency tests whose results were in agree-

ment with the supervisors' findings increased also from 93% to 98%. Of the specimens that were read incorrectly, 72% were false-negative results and 28% false-positive. For smear-positive specimens, the proportion of grading agreement increased from 71% to 92%. The proportion of units achieving a 100% specimen agreement increased from 64% to 79%.

Conclusions and key recommendations: Smear microscopy remains the most cost-effective method of diagnosing pulmonary TB suspects. Conducting proficiency tests is one of the most feasible and effective methods to monitor the technical ability of laboratory staff in proper identification of TB.

PS-100238-14   Operational trial on the introduction of external quality assessment for TB microscopy in West Java

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Setting: TB microscopy service of NTP, Indonesia.

Objective: To provide a systematic review of the progress of 6-month pilot study involving blinded rechecking of randomly selected smear slides from local diagnostic centers and determine its feasibility for future implementation nationwide.

Design: JICA-TBCP introduced the new External Quality Assessment (EQA) employing Lot Quality Assurance Sampling (LQAS) to 13 health centers in 2 districts of West Java since July 2009. The performances of the diagnostic centers, as assessed by the respective EQA laboratories of the districts, are analyzed.

Results: Comparison of results from July and December showed general improvements in smear preparation and reading proficiency of laboratory personnel of the pilot areas as attested by the increase in average proportion of good smears based on 6 checkpoints: Specimen Quality (89%–92%), Staining (85%–95%), Cleanliness (86%–98%), Thickness (75%–86%), Size (71%–77%) and Evenness (72%–86%); decrease of centers showing any type of reading errors (3 to 1) and maintenance of zero major errors in 11 of the 13 centers. Cross-checking workload has remarkably decreased by 53%–84%. Timely feedback and intensified EQA management are crucial factors for improvements.

Conclusion: The new EQA is deemed to be effective for implementation, considering a high TB burden setting. National EQA manual will be revised based on this experience.

PS-101031-14   L'impact de la formation et du bon transport des crachats sur le dépistage des MDR

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Contexte : Depuis 2004, le PNLT-RD Congo a mis en place une prise en charge des malades MDR-TB. Pour leur identification, les échantillons devraient être analysés au LNRM, où la plupart des échantillons n'était pas conforme à la réception, soit renversé, soit sans identité, cela n'a pas permis le dépistage d'assez des cas par rapport aux attentes.

Objectif : Evaluer l'influence de la formation et de l'amélioration du transport des échantillons dans l'augmentation cas des MDR dépisté au LNRM entre 2007 et 2009.

Matériels et méthodes : En 2007, une série de formations sur la prise charge de la tuberculose à bacilles résistants fut organisée dans 4 grandes coordinations pourvoyeuses des patients qui sont : Kinshasa EST, Kinshasa Ouest, Katanga Sud et Province Orientale Ouest. Ensuite un circuit fiable de transports de crachat fut tracé, les moyens de transport financés par l'appui du projet UNION/TBCAP4 et les acteurs à tous les niveaux furent désignés et responsabilisés. Trois ans après, les données des registres furent compilées et analysées.

Résultats : Au total 1124 souches étaient isolées dont 320, 335 et 469 sur respectivement 833 cultures en 2007, 1131 cultures souches en 2008 et 1883 en 2009 soit un accroissement de 31% à 126% en trois ans. Au total 443 MDR étaient identifiés dont 113, 120 et 210 sur respectivement 195 DST faits en 2007, 263 en 2008 et 348 en 2009 soit un accroissement de 6% à 86% en trois ans.

Année	Nombres de cultures	Nombre de souches	Nombre de DST	Nombre de MDR-TB
2007	833	320	195	113
2008	1131	335	263	120
2009	1883	469	348	210

Conclusion : La formation et l'amélioration du circuit des échantillons ont augmenté l'isolement des souches et l'accroissement du dépistage des cas de MDR-TB.

MDR-TB EPIDEMIOLOGY: NORTH AMERICA, EUROPE AND ASIA

PS-100447-14   Prevalence of MDR among retreatment cases in the North West Frontier province of Pakistan

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Objective: To determine the prevalence of MDR and drug resistance pattern among retreatment cases.
Rationale: There is no reliable information available regarding drug resistance pattern in retreatment cases. Study was conducted to determine prevalence and pattern of drug resistance in these cases.
Material and methods: Patient with HO treatment failure of cat-I and Cat-II treatment regimen and with HO relapse after successful treatment of cat-11 were included in the study. Ten district of North West Frontier province were selected based on security situation and convenience in sample transportation to quality assured DST laboratory within 24 hrs of sputum collection. During 9 months sputum were collected from all eligible patients within one week after the declaration of treatment outcome or re-registration of Cat II patients. All collected sputum samples were transported to the designated AKU collection point within one day for culture and DST. Sputum were examined and processed for culture on LJ and Bactec and indirect FL DST was performed by modified proportion method on 7H10 agar. Isolates resistant to R and H were subjected to SLDST.
Result: Total of 139 smear positive patients were enrolled. 120 specimens (86%) were positive on culture. 113 (94.1%) clinical isolates were identified as *M. tuberculosis* which were then tested for drug resistance pattern. Of the 113 positive *M. tuberculosis* isolates 26.5% (30) were from Cat-I failure and 22.1% (25) Cat-II failure and 49.6% (56) cases had HO of relapse after successful completion of Cat-II. 21

Table   Drug-resistant pattern among re-treatment categories

	CAT-I Failure	CAT-II Failure	Relapse after CAT-II	History NA	Total
Total # of strains	30 (26.5%)	25 (22.1%)	56 (49.6%)	2 (1.8%)	113
Susceptible to all FLD	5 (16.6%)	1 (4%)	15 (26.8%)	0	21 (18.6%)
MDR	19 (63%)	19 (76%)	27 (48.2%)	1 (50%)	66 (58.4%)
MDR + OFX resistance	7 (23.3%)	3 (12%)	8 (14.3%)	0	18 (15.9%)
XDR	0	1 (4%)	1 (7.1%)	0	2 (1.8%)

(18.6%) isolates were susceptible to all FLD and 66 (58.4%) were MDR, 18 (27.2%) of the MDR isolates were also resistant to oflaxacin and 2 were XDR cases.
Conclusion: High prevalence of MDR (58.4%) and XDR is seen in retreatment case but significant proportion (18%) is also found susceptible to all FLD. Individual DST is required in all re-treatment cases for clinical management.

PS-100636-14   Ofloxacin resistance in MDR-TB patients in southern Taiwan

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Background: To identify the ofloxacin resistant rate and the factors influencing primary ofloxacin resistance in MDR-TB patients.
Design/methods: Patients diagnosed as MDR-TB between 2007 and 2009 who were admitted to the Taiwan MDR-TB Consortium (TMTC) group in Southern Taiwan. Patients was divided into two groups according to the history of ofloxacin exposure. Group I patients was defined as never exposed to ofloxacin or ever exposed less than one month. Group II patients was defined as ever exposed to ofloxacin more than 1 month. The ofloxacin resistance rate was calculated. The confounding factors like age, gender, comorbidity, severity of disease and category of MDR patients (New case, ever treated with first-line drug, ever treated with second-line drug) was studied by χ^2/Fisher exact test and logistic regression analysis.
Result: A total of 113 MDR-TB patients were included. The primary ofloxacin resistance rate was 16.7% (15/90), secondary ofloxacin resistance rate was 43.5% (10/15), $P = 0.01$. In Group I , the factors influencing primary ofloxacin resistance significantly were young age (<40 years. OR 12.99, $P = 0.008$ compared to age >60 years) and ever treated with second-line drugs before (OR 25.88, $P = 0.002$ compared to new case). There were no difference in ofloxacin resistance rate between the new case and ever treated with first-line drugs.
Conclusion: Ofloxacin exposure was the most confounding factor to ofloxacin resistance. Age less than 40 year-old and ever treated with second-line drug was the risk factors of primary ofloxacin resistance in southern Taiwan.

PS-100681-14   Baseline resistance to second-line drugs among patients with MDR-TB in two Russian regions

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Background: As a part of the US CDC Preserving Effective Tuberculosis Treatment Study (PETTS), the objective of this analysis was to determine the prevalence of resistance to SLDs and risk factors for primary resistance to SLDs among patients with multidrug-resistant TB (MDR-TB) started on SLD therapy in two Russian Green Light Committee (GLC) project sites (Orel and Vladimir).
Methods: MDR-TB patients were consecutively enrolled from 01/2007–12/2008. Drug susceptibility testing (DST) was performed on baseline isolates at the CDC laboratory by the proportion method on Middlebrook 7H10 agar.
Results: A total of 115 MDR-TB patients were included in analysis. Majority were males—96 (83%); median age was 40 years. Cases were classified by prior TB treatment history as: new—42 (38%), treated with first-line drugs only—27 (25%), and treated with SLDs—41 (37%) of 110 patients with known treatment history. Overall, 38 (33%) of 115 isolates had resistance to kanamycin, 19 (17%) to amikacin, 8 (7%) to capreomycin, 20 (17%) to ofloxacin, 19 (17%) to ciprofloxacin, 16 (14%) to ethionamide, 18 (16%) to PAS, and 72 (63%) to rifabutin. Resistance to all four first-line drugs was found in 62 (54%) of isolates; resistance to at least one SLD in 63 (55%); resistance to at least one injectable SLD in 40 (35%); resistance to all three injectable SLDs in 6 (5%); resistance to any fluoroquinolone in 21 (18%); and 13 (11.3%) had extensively drug-resistant (XDR)-TB. Among 42 new MDR-TB cases, 22 (52%) had any SLD resistance (primary). The only risk factor significantly associated with primary SLD resistance among new MDR-TB cases ($n = 42$) was female gender (PR = 1.75, 95%CI 1.03–2.96).
Conclusion: The prevalence of resistance to SLDs was high among those with MDR-TB in Orel and Vladimir, and 11% had XDR-TB.

PS-101054-14   First results of MDR Survey in Tajikistan

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Background: The first Drug Resistance Survey in Tajikistan was conducted in 2008 in two pilots: Dushanbe and Rudaki with total population 994 200 (2007) or 14% of the total population of Tajikistan. The survey duration was April 2008 to March 2009.
Methodology: In total 372 new and retreated SS+ TB patients were tested by NRL in Dushanbe. Results of 288 TB patients meeting enrollment criteria, 150 new and 138 retreated cases were received. Positive cultures were sent to SRNL in Gauting, Germany for DST for first and second line TB drugs.
Results: 110 out of 288 tested patients had confirmed MDR (26 among new and 83 among retreated SS+ cases). MDR-TB rates is 17.4% for new cases and 67.2% for previously treated cases. Among 110 MDR strains, only 4 strains have HR pattern (from 1 new and 3 previously treated patients). The most common MDR patterns were HRES, found in 70 cases (15 new and 55 previously treated) and 35 HRS (10 new and 25 previously treated. The age and sex structure of MDR-TB patients was similar to the group of patients with any resistance, majority of MDR cases grouped in younger age groups 15–35. This study revealed 25 XDR cases, 21 previously treated and 4 new TB cases.
Conclusion: One of the basic reasons of high MDR rate in the country is inadequate DOT that is evidenced during monitoring visits. MoH has to undertake adequate measures to improve DOT as MDR-TB prevention.

PS-100060-14   Trends of primary drug resistance in Republic of Moldova

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Setting: The resistance to TB drugs represents a serious obstacle to effective control of the TB epidemic in Moldova. The results of drug resistance surveillance can reflect the indicators of tuberculosis (TB) control programme efficacy. Primary drug resistance, particularly multidrugresistance (MDR) is one of the main causes of ineffective treatment of new TB cases.
Aim: To estimate the trends of primary drug resistance in Republic of Moldova during the period of DOTS implementation (2003–2008). The results of drug susceptibility test (DST) to I line anti-TB drugs

among new (never previously treated) TB cases of civil and penitentiary sector were studied.

Materials and methods: Surveillance of drug resistance included all isolates from new patients diagnosed with pulmonary TB during the last 6 years. The DST was performed in the National Tuberculosis Reference Laboratory from Chisinau and three Regional Tuberculosis Reference Laboratories (Balti, Vorniceni and Benderi) on L-J media using absolute concentration method. External quality control for DST was conducted by the Supranational reference laboratory from Borstel, Germany.

Results: The prevalence of the anti-TB resistance in the R. Moldova increased considerably during the last 5 years. In the performed study it was analysis of 4517 results of drug sensitivity tests performed in these laboratories. The level of primary drug resistance has been increased from 20.5 to 42.9% during this period, and MDR-TB from 6.0% to 24.9%. Trough patients with MDR-TB were identified 7% cases with extensively drug resistant.

Conclusion: At the current stage the primary drug resistance of TB is a serious problem in the R.Moldova, having serious public health and economic consequences. The increase number of resistant cases influences of the treatment results. The accumulation of a greater number of resistant strains in society can lead to the infection of population and increase the number of resistant TB.

PS-100272-14 Drug resistance in tuberculosis, study from Gujarat, India

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Purpose: Because of the emergence of multidrug-resistant tuberculosis in recent times, to determine the precise prevalence rate and pattern of Drug resistant in Previously treated (Acquired drug resistant) and First time diagnosed (Primary and Initial drug resistant) in patients from Gujarat, Rajasthan and Madyapradesh.

Material and methods: Total number of 96 culture positive specimen are included in study and tested for Anti tubercular drug susceptibility testing against First line and Second line Anti tubercular drugs by Resistant Ration method. 96 Culture positive Patients are classified in two groups, 66 Culture positive patients had received anti tubercular treatment in past and prevalence of resistant is (acquired drug resistant) is determined and they further classified as MDR and XDR cases and 30 Culture positive patients are newly diagnosed patients and prevalence of drug resistant is determined (Primary and Initial drug resistant).

Results: Among the 66 Previously treated patients' stain (All are MTb complex) 53 (80.30%) has resistant to one or more Anti TB drugs, 34 (51.51%) clas-

sified as MDR cases and 4 (6.06%) classified as XDR cases. Among 30 newly diagnosed patients' strain 2 were NTM (non-tuberculous mycobacteria and 28 were *M. tuberculosis* complex, 07 (25.0%) has resistant to one or more Anti TB drugs, 03 (10.71%) classified as MDR cases and 0 (0.0%) classified as XDR cases.

Conclusion: High prevalence of acquired multi drug resistance (MDR), extensively drug-resistant tuberculosis (XDR) and primary & initial multidrug resistance (MDR) in community, accurate susceptibility testing is necessary to identified the multidrug resistance Tuberculosis cases and by having susceptibility pattern prevent the conversation of MDR cases into XDR cases.

PS-100434-14 Multidrug-resistant tuberculosis in Cuba, 2000–2008

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Aim: The spread of multidrug-resistant tuberculosis (MDR-TB) in the world remains a major public health problem. Surveillance of anti-tuberculosis drug resistance is therefore as essential tool for monitoring the effectiveness of TB control program and, through policy development, for improving national and global TB control. The objective of this work was to determine the prevalence of MDR-TB in Cuba during the period 2000–2008.

Method: Drug susceptibility testing was determined in 2081 Mycobacteriun tuberculosis strains against isoniazid, rifampicin, streptomycin and ethambutol. The tests were conducted using the proportion method on Löwenstein-Jensen medium according to the standard procedures.

Results: Multidrug-ressitant was identified in 5 (0.27%) of 1870 patients in new cases. Among patients who had received prior treatment, 22 (10.4%) showed MDR.

Conclusions: The early application of DOT and surveillance of drug-resistance by the Cuban National Tuberculosis Control Programme has resulted in the decrease of *M. tuberculosis* with resistance among new cases and very low rates of MDR-TB. The results have set the stage for the possibility of TB elimination in Cuba.

PS-100521-14   Impact of expanded surveillance of XDR- and MDR-TB, United States, 2000–2007

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Background: State TB programs report initial and final drug susceptibility (DST) results for culture-confirmed TB cases to the National TB Surveillance System (NTSS) in the United States. Our goal was to determine whether expanded reporting of DST results would increase identification of extensively drug resistant (XDR) TB (resistant to one fluoroquinolone and one second-line injectable medication) and multi-drug-resistant (MDR) TB cases.
Methods: The TB programs of California, Florida, New York City, and Texas developed a pilot registry to collect all DST results, including results on additional fluoroquinolones (levofloxacin and moxifloxacin) and second-line injectable medications, for MDR-TB cases reported in their jurisdictions from January 1, 2000 to June 30, 2007.
Results: Among 589 cases included in the pilot registry, 25 (4%) were XDR-TB. MDR-TB cases with the appropriate DST results to evaluate for XDR-TB increased from 82% in NTSS to 93% in the pilot registry. Six cases previously reported in NTSS as MDR-TB were reclassified as XDR-TB based on additional DST results. Sixteen MDR-TB cases in the pilot registry had isolates resistant to levofloxacin or moxifloxacin when no fluoroquinolone testing was reported in the NTSS. Four MDR-TB cases reported in NTSS with isolates susceptible to ciprofloxacin or ofloxacin were identified as resistant to levofloxacin or moxifloxacin. No additional XDR-TB cases were identified based on second-line injectable susceptibility testing.
Conclusion: Reporting all DST results, including additional reporting of fluoroquinolone resistance, to the NTSS will result in a more accurate count of XDR-TB or MDR-TB cases in the US.

PS-100527-14   Drug resistance surveillance on tuberculosis in Xinjiang

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Objectives: To understand the magnitude and pattern of drug resistance in Xinjiang; to evaluate the effectiveness of TB control program; and to provide scientific basis for formulating and revising related policies.
Methods: According to WHO/Union 'Guidelines for Drug Resistance Surveillance of Tuberculosis', 30 clusters were randomly selected with stratified cluster sampling by experts from WHO and national reference laboratory. The sample size for new smear positive cases was calculated as 1470. Each of 30 clusters was required to continuously intake 49 new smear positive cases, and all the re-treatment smear positive pulmonary tuberculosis patients at the same time period should be involved for investigation as well.
Results: 1) Among total 1700 involved cases, 1083 (63.7%) have DST result for analysis, including 969 new cases and 114 re-treatment cases. No NTM (non-tuberculosis mycobacteria) found. The main reason of such a low percentage of usable strains is contamination due to long term storage of isolates before DST was done. 2) From the survey we found that in Xijiang, drug resistant rates were 25.9% and 30.7% in new cases and previous treated cases respectively; MDR rate was 4.2%, 7.9% and 4.6% for new, re-treated and overall; and resistance ranking by drug was: S (17.1%), H (11.8%), R (8.0%) and E (2.1%).
Conclusions: The prevalence of drug resistant tuberculosis is rather high in Xinjiang, and the quality of TB control performance need to be strengthened.

PS-100652-14   The development of drug resistance in TB patients in some regions of Kazakhstan

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Setting: In XXI century the situation of TB in the world complicated by the growth of TB patients with drug-resistance (DR). In Kazakhstan, since 1998 implemented National TB programs (NTP), recommended by WHO, which led to a decrease of the incidence, prevalence (47%) and mortality (2 times). At the same time, there was an increase of the number of patients with MDR-TB, so the incidence of MDR-TB was 8.5 per 100 000, the prevalence of MDR-TB—9, 8 per 100 000 (2008). This problem requires the efforts of NTP to identify the causes of development of MDR, which will take measures for its reduction.
Aim: To study the effect of DR on the outcome of the disease in TB patients in Almaty area and city at the different stages of the disease.
Material and methods: Retrospective and descriptive analyses of 795 patients with unsatisfactory results of the two courses of treatment held in the studied regions (2006–2009).
Results: There were men (584/74.6%), of the most employable age (377/77.9%) and with low socio-economic status (749/94.3%) among all cases. At the stage of new TB cases' sputum (479 patients) was cultured and tested for drug sensitivity and estimated any DR (35/7.3%), MDR (26/5.4%) before treat-

ment. At the stage of repeated TB cases (655 patients), of whom relapse is defined in 231 (35.3%), failure of treatment in 140 (21.4%), interrupted treatment in 38 (5.8%) and others in 236 (37.6%). Acquired DR was set in 305 (46.7%), MDR in 144 (22%) cases. At the stage of the status of the patient with unsatisfactory results after two treatments DR determined in 554 (72.4%) including MDR in 400 (50.3%) and XDR in 24 (3%). In 386 (48.6%) TB patients identified poor prognosis of the disease, death, which is associated with DR in ½ of cases.

Conclusion: The unsatisfactory results of the two courses of treatment TB cases were related with acquired DR (72.4%) and MDR (22%). Unfavorable prognosis of outcomes ½ of TB cases associated with the presence of any DR.

PS-100780-14   Screening of MDR for the prevalence of XDR in selected communities of Bangladesh

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Aim: Screening of multidrug-resistant (MDR) *Mycobacterium tuberculosis* strains for the prevalence of extensive drug resistance (XDR) in the community.
Method: *M. tuberculosis* strains were isolated from tuberculosis (TB) suspects following conventional culture technique. Proportion susceptibility testing (PST) method was followed for the selecting strains with multidrug resistant (MDR) phenotypic, which were further characterized for the detection of mutations at *rpo*B, *Kat*G, *inh*A genes by sequencing. Strains were tested for resistance to kanamycin (KM) and O-floxacin (O-fl) by PST method. Spoligotyping was performed to find out the prevalence of different phylogenetic clades.
Results: Majority of the strains had mutation at *rpo*B and *kat*G genes. Of 92 phenotypic MDR, monoresistance was detected in 5% strains to kanamycin and in 2% to O-flo. Unique spoligo patterns were detected in 24 strains and 68 strains were grouped into Beijing ($n = 24$), Central Asian ($n = 18$), East African Indian ($n = 7$) and Principal Genetic group 2 & 3 ($n = 19$).
Conclusion: MDR strans were genotypically heterogenous possibly happened as result of reactivation of past infection as well as recent infection. Strains monoresistance to either Km or O-fl may acquire resistance simultaneously to both KM & O-fl to become XDR. This study indicates emergence of XDR among MDR strains in the rural and urban community of Bangladesh.

PS-100958-14   DR TB surveillance in Russia: improving quality of data from routine TB laboratory service

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Background: Among high multidrug resistant tuberculosis (MDR-TB) burden countries the Russian Federation (RF) has one of the most comprehensive DR TB routine surveillance system (DRRSS). This routine system notifies 49% of MDR-TB among new TB cases (NC) in the world while WHO Global estimation accounts 7%. Evaluation of quality and completeness of Russian DRRSS data is relevant for understanding input of RF to the global MDR-TB threat.
Methods: 2007–2008 data of DRRSS were collected and analyzed using Russian DOTS cohort and prevalence reporting forms, as well as adapted WHO criteria for evaluation and grading of regional DRRSS. Grading criteria for 2 groups of regions ('A' and 'B') included: (1) not less than 95% accuracy of DST tests for RMP and INH for labs covering 50%–75% ('A') and ⩾75% ('B') of NC notified in the territory, (2) culture confirmation 35%–50% ('A') and ⩾50% ('B'), (3) appropriate level of ss+ confirmation of cavitary TB (SCCV).
Results: DRRSS has notified 14% of MDR-TB among NC (2008) which was closed to WHO estimation (15.8%). Registered prevalent MDR-TB cases in the Russian Federation (2008) represents 86.8% of WHO estimation of all MDR-TB cases.
Number of regions met grading criteria of DR data 'completeness' has reached 20 from 6 in 2008 (4th DR WHO report). Nine of them have shown a decrease of MDR-TB among NC in 2007–2008. 12 Oblasts, met 'A' criteria, has shown 17% as the median of MDR-TB among NC (Q25:13.7%; Q75: 20.9%). The regions demonstrate quality of all process of TB lab diagnostic: Culture confirmation rate of NC and DST coverage among them were respectively 56.7% (54.3%; 69.8%) and 98.2% (vs. RF: 37.2% and 91.1% accordingly, $P < 0.001$), and SCCV was 70.8% (vs. RF: 57.9%, $P < 0.001$).
Conclusion: Improvement of lab DST procedures and standardization of data flow between lab and epi-surveillance registers has contributed to gradual increase of number of regions with quality DRRSS and consequently to DRRSS improvement itself.

PS-101219-14   Multi drug resistant tuberculosis in a referral hospital of Bangladesh

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Background: Though government has been successful in achieving the WHO target of the DOTS program, tuberculosis control is threatened by the emergence of drug resistance strains. A large number of patients come to the most specialized chest disease hospital in Bangladesh with the relapse of TB. This study investigated the prevalence, patterns and risk factors of drug-resistant *Mycobacterium tuberculosis* at a tertiary referral hospital in Bangladesh.

Methods: TB patients admitted at National Institute of Diseases of the Chest and Hospital (NIDCH) from February 2002 to September 2005 with previous history of tuberculosis and/or other complications were interviewed. *M. tuberculosis* isolates from 189 patients were tested for susceptibility to rifampicin, isoniazid, ethambutol and streptomycin using the proportion method.

Results: Of the 189 *M. tuberculosis* isolates, 9% were fully susceptible to the 4 primary drugs and 73.5% were resistant to both isoniazid and rifampicin (multidrug-resistant TB [MDR-TB]). Other susceptibility results showed 79%, 79%, 77% and 77% resistance to isoniazid, rifampicin, ethambutol and streptomycin respectively. Multidrug resistance was significantly higher among the patients with previous history of anti-tuberculosis treatment (95% confidence interval, $P = 0.001$). Less compliance with treatment is also observed in this group.

Conclusion and recommendations: The high rate of MDR-TB was associated with previously incomplete anti-tuberculosis treatment. Proper counseling of patients and attention towards the completion of the anti-TB treatment are needed to prevent the relapse as well as drug resistance. In TB prevalent areas, a drug susceptibility testing should be carried out among the patients having the past history of anti-TB treatment.

PS-101466-14   Surveillance of tuberculosis drug-resistant in upper north of Thailand

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Background: Drug resistant tuberculosis is an emerging problem in many part of the world. In Thailand, several studies were done to determine this situation but not in a systematic way. The average of multidrug-resistant tuberculosis (MDR-TB) rate was 0–10%.

Objective: To study the prevalence of multidrug-resistant in upper north of Thailand.

Method: Cross sectional study in tuberculosis suspected patients who came to public hospitals in 8 upper northern provinces. All cases who had sputum smear positive from April 2008 to September 2009 were sent to Central Laboratory, Office of Disease Prevention and Control 10th for culture and drug susceptibility test (DST). DST was done against 6 standard anti-tuberculous drugs by proportional method which was recommended by the National Committee for Clinical Laboratory Standard (NCCLS). Non-tuberculous mycobacteria were excluded from this study.

Results: DST was done in 2067 patients. Drug resistant was found in 665 (36.8%) patients. One, two, three and four drugs resistant was 27%, 4%, 0.8% and 0.6% respectively. MDR was 3.5% and extensively drug resistant tuberculosis (XDR-TB) was 0.3%. If NTM infection was not excluded, MDR rate will increase to 11.1%.

Conclusion: Drug resistant rate in upper northern region of Thailand was very high especially MDR rate which was higher than 3% as WHO suggested to implement DOTS plus because that area is a hotspot of MDR. Drug resistant surveillance, culture with DST and rapid identification should be implemented in this region to improve quality of tuberculosis case management.

PS-100184-14   Risk factors for MDR-TB in Nepal: a matched case control study

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Introduction: Nepal has been implementing a MDR-TB case management DOTS-PLUS Program since 2005. 659 cumulative cases were registered up to the end of 2009. Increasing numbers of cases are being detected. Cases are increasing rapidly and it is important to understand the risk factors for the development of MDR-TB.

Objective: An epidemiological study to explore the risk factors for MDR-TB in Nepal by Matched Case Control Study.

Methodology: From different regions, a case control study with ratio of 1:2 was carried out and 55 cases and 110 controls were selected under study using standard formula. MDR-TB patients on treatment in clinic were enrolled as Cases and Controls were age, sex matched cured TB patients who had completed treatment in the same centre with same ecological zones. Data was collected by a trained research assistant using interviewer administered structured ques-

tionnaire. And analysis was done using SPSS 13 version and logistic regression model were used for data analysis.

Results: The following were the significant risk factors for MDR-TB in Nepal: Marital status Odds Ratio (OR) = 2.1 (95%CI = 1.07–4.01); employment status, OR = 4.3 (95%CI = 2.1–8.7), contact history of TB, OR = 4 (95%CI = 2.0–7.9); HIV status, OR = 15.9, (95%; CI = 1.92–133); type of family, OR = 3.77 (95%CI = 1.58–9.05), place of living, OR = 3.5 (95%CI = 1.77–3.67). The following were not statistically significant: religion OR = 1, (95%CI = 0.4–2.5); literacy status OR = 0.65 (95%CI = 0.31–1.38); smoking status, OR = 1.10, (95%; CI = 0.5–2.4); family income, OR = 1.53 (95%CI = 0.78–3.03); types of fuel used for cooking, OR = 0.63 (95%CI = 0.32–1.25).

Conclusion: These results provide information to guide program planning and management in policy level.

PS-100638-14   Prevalence of multidrug-resistant tuberculosis in the Arkhangelsk region, Russia

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Background: In 2000–2009 TB incidence in the Arkhangelsk Region decreased from 104/100 000 to 55.2, TB mortality from 16.5 to 8.0, but MDR-TB prevalence increased from 12.1 to 34.8. MDR treatment was increasingly provided but not to all until 2008 with GLC approval.

Intervention: Trends in incidence and prevalence were assessed for the period 2006–2009. MDR incidence was monitored according to WHO Guidelines while MDR prevalence was defined as the number of registered MDR cases with active disease at the end of each year.

Results: The number of prevalent MDR-TB patients declined from 565 in 2006 to 436 in 2007 but did not decline further: 434 in 2008 and 439 in 2009. Incident MDR cases did not decline: 181 in 2006, 208 in 2007, 182 in 2008 and 196 in 2009. New MDR-TB cases increased from 103 in 2006, to 124 in 2007, 113 in 2008 and 131 in 2009 (from 57 to 67% of incident MDR cases). Previously treated cases with MDR-TB declined from 43% to 33% of incident cases: Relapses from 70 to 70, 51 and 54. MDR-TB after default declined from 6.3% to 2.6% and patients treated after failure increased from 1.1%, to 3.0%.

Conclusion: Sustained prevention and treatment of MDR-TB are needed over several years before MDR prevalence declines, ensuring high coverage of treatment.

PS-101378-14   Association between MDR-TB and sex

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Background: In most countries, the large majority of TB patients are male. However, differences in access to health-care services or exposure to other risk factors may result in male or female TB patients having different levels of drug resistance.

Intervention: In 2008 a total of 38 countries and 3 territories provided to WHO drug resistance surveillance data stratified by sex. Of them, 27 countries and 2 territories reported at least one case of MDR-TB among male and female cases.

Results: After adjusting for the clustering effect at the country level the overall odds ratio of being an MDR-TB case in female cases compared with male cases was 1.1 (95%CI 0.9–1.4), showing no overall association between MDR-TB and the sex of the patient. In South Africa, data from a total of 81 794 TB patients with known sex (95% of all patients) indicate that female TB cases have a 1.2 times higher odds (95%CI 1.1–1.2) of harbouring MDR-TB strains than male TB cases. Data from Australia (OR 2.7, 95%CI 0.9–8.7), the Netherlands (OR 0.7, 95%CI 0.5–0.9) and the USA (OR 3.2, 95%CI 0.9–14.3) also show a higher risk of MDR-TB in female patients. Conversely, in Lithuania the odds are lower for female patients of having MDR-TB (OR 0.7, 95%CI 0.5–0.9).

Conclusions: While males predominate among TB cases in most countries, this analysis suggests that the association between sex and MDR-TB strains, when present, is small. This relationship may be confounded by factors which are associated with sex, such as alcohol misuse and imprisonment. Determining whether females or males are more likely to have MDR-TB provides insight into the epidemiology of the disease, allowing for the development of targeted measures to improve access to care or reduce the risk of acquiring drug-resistant strains.

PS-101382-14   MDR-TB in relapse cases

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Background: Prior exposure to anti-TB drugs is a well-known risk factor for drug resistance, as repeatedly shown in surveys and surveillance worldwide. Previously treated TB cases are a heterogeneous group composed of relapse cases, cases having failed one or more treatment regimens using first-line and/or second-line drugs, cases returning after treatment default, and others. Patients failing treatment are known to have greater risk of harbouring multidrug resistant

TB (MDR-TB) strains. Sporadic reports suggest that proportions of MDR-TB are also higher in relapse cases. In this analysis we investigate the proportion of MDR-TB in relapse cases and compare it to that in new cases.

Intervention: In 2008, 17 countries conducting continuous surveillance reported MDR-TB proportions disaggregated by relapse and new cases.

Results: Among the 10 countries that reported at least one case of MDR-TB among new and relapse cases, the proportion of MDR-TB among new cases was 1.5% (95%CI 0.5–2.6) and among relapse cases 7.9% (95%CI 2.9–12.9). Relapse cases combined from all 10 sites had a 5.5 times higher odds of harbouring MDR-TB strains compared with new cases (95%CI 4.4–6.8), after adjusting for the clustering effect at the country level.

Conclusions: Relapse cases have a significantly higher risk of MDR-TB compared to new cases. This may suggest frequent reinfection with drug resistant strains during previous hospitalizations in settings with inadequate infection control measures, or alternatively weaknesses in treatment delivery and/or methods for declaring a patient successfully treated. Diagnostic drug susceptibility testing should be made available to those patients to be able to offer more adequate regimens since the beginning of the re-treatment.

NON-TUBERCULOUS MYCOBACTERIA

PS-100289-14   Cord-factor of *Mycobacterium simiae*: strain 'Habana' TMC 5135, as inductor of TNF-alpha

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The structure of cord-factor of *Mycobacterium simiae* ATCC 25275T, *M. simiae* ('habana') IPK-342 and *M. simiae* ('habana') TMC 5135 (the last one considered highly immunogenic in experimental tuberculosis and leprosy) was studied employing NMR and MS techniques. The expected general composition 6,6′-dimycoloyl trehalose was found in all cases. Variations among strains were detected on mycolic acids (a′, a and keto) liberated from cord-factor and on some fine details revealed by NMR. Notably, the strain TMC 5135 presented a distinctive 1H-NMR spectrum and contained high levels of trans-cyclopropanation (mainly C87 and C89 a- and keto-mycolic acids), whereas mycolic acids from cord-factor of ATCC 25275T and IPK-342 contained high proportion of a′-mycolates, together equilibrated amounts of even

(mainly C84, C86) versus uneven (mainly C87, C89) a-mycolic acids. In general, mycolic acids from cord-factor of the strains investigated tended to be slightly longer and with less trans-cyclopropanation than those found in its respective delipidated cells. Cord-factor from TMC 5135 was able to induce, at various amounts, the secretion of TNF-α in the cellular line RAW 264.7, unlike ATCC 25275T and IPK-342. The results indicated that cord-factor from TMC 5135 presents some specific fine structural details that seem to be related to its capacity of induction of TNF-α. These findings could explain, in part, the immunogenicity demonstrated by others for strain 'habana' TMC 5135.

PS-100846-14   Species identification of nontuberculous mycobacteria using GenoTypeCM and GenoTypeAS

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Standardization of reference nontuberculous mycobacteria strains (NTM) for laboratory collections is very important task. Microbiological methods for species identification of NTM have been used for several decades. However microbiological tests are not accurate and require long time. To verify results of microbiological tests for identification of NTM strains from CTRI collection molecular-genetic method GenoTypeCM/GenoTypeAS (HAIN Lifescience) were used. 26 NTM strains from CTRI collection were taken into the study (5 strains of *M. avium*, 3 *M. intracellulare*, 1 *M. battey*, 2 *M. fortuitum*, 1 *M. peregrinum*, 1 *M. gastri*, 3 *M. kansasii*, 1 *M. marinum*, 2 *M. phlei*, 1 *M. runyoni*, 1 *M. simiae*, 2 *M. smegmatis*, 1 *M. xenopi*, 1 *M. chelonae*, 1 *M. scrofulaceum*). Preliminary identification was carried out using microbiological methods in 1960–1980. Results of molecular-genetic identification confirmed results of microbiological tests in 21 strains from 26. Of these 21, 2 strains have mismatch in species name: *M. battey* (old species name for *M. intracellulare*) = *M. intracellulare* according to GenoTypeCM/AS; *M. runyoni* (old name for *M. chelonae*) = *M. chelonae* subsp. abscessus. Microbiological species identification was incorrect in 5 strains. *M. marinum* proved to be *M. smegmatis* according to GenoTypeCM/AS, 1 strain *M. phlei* proved to be *M. smegmatis*, 1 strain *M. kansasii*—*M. avium*, *M. chelonae*—*M. intracellulare*, 1 strain *M. smegmatis*—*M. intracellulare*. Thus it is not enough to carry out only microbiological testing for species identification of NTM. It is necessary to use molecular-genetic methods for correct and rapid species identification of NTM.

PS-100969-14   Mass spectrometry based methods for the discrimination and typing of mycobacteria

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Discrimination of *Mycobacterium tuberculosis* complex and non-tuberculous mycobacteria (NTM) is very important for diagnostic purpose and susceptibility testing. Further spoligotyping based on analysis of direct repeat region (DRR) is considered as reproducible and standardized method for MTC epidemiology. In this study we demonstrated the complex solution based on MALDI ToF MS suitable for rapid and accurate species identification and typing of mycobacteria. For direct MALDI ToF MS analysis, mycobacterial cells grown on Löwenstein-Jensen medium were transferred into 300 μl of water. After precipitation with ethanol (900 μl) and centrifugation, the pellet was added with 20 μL of 35% formic acid, 50% acetonitrile and analyzed by an AutoflexTM (Bruker Daltonik GmbH, Germany) mass spectrometer with α-CHCA as a matrix. For spoligotyping amplification of DRR was done according to standard protocol. The structure of DRR was discovered by primer extension reaction followed with MALDI ToF MS using 3-HPA as a matrix. The development techniques were tested on the mycobacterium collection representing 2 species belonged to MTC (~400 strains) and 13 species of NTM (~40 strains). For 67 strains direct MALDI-ToF MS profiling was done. While minor differences was caught between *M. tuberculosis* and *M. bovis*, the mass spectra collected for NTM (*M. avium, M. intracellulare, M. chelonae, M. gordonae, M. kansasii, M. gastri, M. deirnhoferi, M. fortuitum, M. peregrinum, M. smegmatis, M. phlei, M. simiae, M. neoaurum, M. lentiflavum*) were undoubtedly diverted them according to their species belonging. For MTC spoligotyping 43 spacer-specific primers combined into 8 multiplex were selected, that allows to detect all spacers for each isolate. The results obtained by suggested method were completely confirmed by classical spoligotyping data. Novel reproducible and efficient approaches based on the MALDI MS were developed for the discrimination and typing of mycobacteria.

PS-101290-14   Nontuberculous mycobacteria pulmonary disease in Peru: case report

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Background: Non-tuberculous mycobacteria (NTM) pulmonary disease is highly complex in terms of clinical presentation and management. Its clinical features are indistinguishable from those of pulmonary tuberculosis (TB).
Aim: To describe clinical findings of NTM pulmonary disease cases identified in National Tuberculosis Program from Peru.
Materials and methods: We reviewed clinical, microbiological and radiological features of 8 cases of NTM isolated by Mycobacteria Laboratory of National Institute of Health from Peru, reported from 2007 to 2009.
Results: Regarding to demographic characteristics 4 were males, the mean age was 57.12 ± 15.11 years, 62.5% were from the equatorial region of Peru. From total cases there was a smoker patient, other with skin cancer, no one with HIV or another immunosuppressive disease. All of these cases had had at least one previous episode of TB (1.14 ± 0.84). NTM disease was diagnosed after 2 years of TB episode (2.62 ± 3.07 years). The main symptoms were cough and weight loss (82.5% and 37.5%). The main radiological findings were fibrosis, cavities, bronchiectasis (82.5%, 62.5% and 37.5% respectively). 3 cases of *M. chelonae* and 2 of MAC were identified. All of them were initially managed like MDR-TB. There were four cases with extended resistance to antituberculosis drugs in DST. Five cases are still in treatment.

Table Characteristics of NTM cases reported to NTS from Peru

Characteristic	N° (8)
Age, years ± SD	57.12 ± 15.11
>60 years	4 (50%)
Cough	7 (82.5%)
Loss of weight	3 (37.5%)
Radiological findings	
Fibrosis	7 (82.5%)
Cavities	5 (50%)
Bronchiectasis	3 (37.5%)
NTM	
M. chelonae	3
MAC	2
Therapeutic condition	
In treatment	5
Death	1
Treatment completed	2

Conclusion: NTM disease could be clinically confused with MDR-TB. NTM is present in people with previous episode of TB. NTM have an extended resistance to antituberculosis drugs.

PS-101497-14 Phenotypic and molecular study of mycobacteria fast-growing interest in public health

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Mycobacterium chelonae—M. abscessus and *M. fortuitum—M. peregrinum* complexes are composed by bacterial species characterized by rapid grow and considered as potential pathogens. These microorganisms are ubiquitous in the environment, resistant to water treatment such as standard chlorination and are able to replicate even at poor nutrient conditions. They are related to lung and extra-lung infections in immune-compromised patients or those submitted to invasive surgical procedures. The aim of this study was to confirm the identification of *M. chelonae—M. abscessus* and *M. fortuitum—M. peregrinum* complexes, isolated from biological samples considering one or two repetitions if samples are originated from sterile or non-sterile site respectively. Phenotypic tests and molecular methods, PRA-*hsp*65 and *rpo*B gene sequencing, were applied to identify 38 strains previously isolated. Results demonstrated that available phenotypic tests did not allow the identification of all described fast-growing mycobacteria. The PRA of *hsp*65 gene confirmed the identification of 63% of the mycobacteria studied, and demonstrated the band pattern shared by *M. abscessus* 2, *M. bolletii* and *M. massiliensis*. The *rpo*B gene sequencing confirmed the identification of the species cited. Our results demonstrated that PRA-*hsp*65 and *rpo*B gene sequencing are useful tools to provide a more accurate species identification of mycobacteria. The use of such techniques would be considered in reference laboratories to identify fast growing mycobacterial species since they are considered emerging pathogens implicated in outbreaks and isolated from a patient in reference centers for treatment of multidrug-resistant tuberculosis.

PS-100997-14 *Mycobacterium habana*: virulence, immunogenicity and protection against experimental tuberculosis

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Background: *Mycobacterium habana* was isolated in Cuba in 1971. Later, was demonstrated its protection capacity against mycobacterial experimental infection.
Methods: Virulence of *M. habana* was assessed using a progressive pulmonary TB model. In the second assay, mice were vaccinated with live bacilli; immunogenicity was related with in vitro IFN-γ production. Best doses were used for animal vaccination. Two month later, challenge was done with *M. tuberculosis* H37Rv and Beijing genotype.
Results: *M. habana* TMC-5135 and IPK-337 infected animals showed 100% survival in contrast with 20% of death with IPK-220. All mice received H37Rv were died to 9 weeks post-infection. Histopathological findings showed that granuloma area in recipients of IPK-337 and TMC-5135 increased significantly throughout the experiment. Pneumonic patches represented less than 10% of lung surface. Because of no significative differences were observed between IPK-220 and H37Rv groups, IPK-220 was discharged it for the coming experiments. Doses of 2500 and 8000 bacteria of IPK-337 and TMC-5135, respectively, were selected due to the higher induction of IFN-γ. Protection induced in mice vaccinated either *M. habana* or BCG strain and challenged with H37Rv showed no statistical differences. However, Beijing challenge showed statistical differences in the survival rate between vaccination with TMC-5135 and BCG. This last group exhibit more than 70% of pneumonia and lower granuloma area. CFU recovered in recipient of TMC-5135 were 1.5 times lower than BCG group.
Conclusion and recommendations: Vaccination with live *M. habana* induces immunological protection against experimental tuberculosis infection. Further studies including nude animal models will be carried out.

PS-100523-14 Evaluate the isolation rate, drug susceptibility test and clinical features of *M. kansasii*

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Background: The incidence of diseases caused by non-tuberculous mycobacteria (NTM) is increasing worldwide. According to the report of National Taiwan General Hospital, the isolation rate of NTM had also increased from 19.5% in 1997 to 31.9% in 1999 in Taiwan. *M. kansasii* is the most virulent opportunity pathogens among NTM. It can lead to pulmonary or disseminated infections in HIV patients, and noncavitary nodular disease of bronchiectasis and fibrocavitary lung diseases in non-HIV patients. If *M. kansasii* remains untreated, it might cause lung disease. The aim of this research was to investigate the drug resistant problems for *M. kansasii*, potential effect of clarithromycin and the clinical characteristics including radiographic features and treatment outcomes in Taiwan.

Method: All clinical specimens of *M. kansasii* in Tai-chung Veterans General Hospital (TC-VGH) between January 2004 and December 2006 were collected. All specimens were isolated and identified with BDProbeTec, and drug susceptibility tests with agar proportion method and E-test strip were performed. The strains were classified using *hsp65* PCR-restriction assay. The subjects' clinical and demographic data were collected for analysis.

Results: The isolation rate of *M. kansasii* was only 1.9% (41 isolates). The common comorbidities were chronic respiratory disease (57.7%) and HIV infection (26.9%). Except for the low concentration of isoniazid (0.2 g/mL), all compounds including high level of isoniazid, ethambutol, streptomycin, rifampicin and clarithromycin showed excellent (>85%) results in vitro activity. Genotype I (82.5%) was the most common subtypes found and mostly involved with right upper lobe. 12 patients (46.2%) received antimycobacterial therapy of isoniacid, ethambutol and rifampicin for 6–9 months. The results were 9 success, 1 failed and 2 died.

Conclusion: Clarithromycin is a possible alternative drug for improving the treatment of *M. kansasii* especially when there is drug intolerance.

PS-100908-14   Prevalance of non tuberculous mycobacteria in and around Johannesburg, South Africa

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Introduction: *Mycobacterium tuberculosis* is the major cause of lung disease but non-tuberculous mycobacteria (NTM) are emerging as true pathogens.

Objective: To analyse the prevalence of NTMs and determine which are the most prevalent and if they are clinically significant.

Method: Prevalence of NTM at the Mycobacteriology Reference Laboratory between the period of January 2009 and June 2009 was analysed by using laboratory data. This laboratory receives all TB culture specimens from all around Johannesburg. All potential positive from MGIT and MycoF-Lytic bottles are confirmed by the Ziehl Neelson stained slide of the culture. All cultures that do not resemble *M. tuberculosis* are sent for MOTT (NTM) identification. The tests for identification currently employed are:

- CM for positive MGIT cultures
- The Accuprobe (Genprobe) for MycoF-Lytic cultures
- Biochemical testing.

Results: Total positive cultures = 2191. 392 contaminated, 40 failed to grow. 640 *M. intracellulare*, 295 *M. avium* complex (MAC), 217 *M. avium*, 113 *M. fortutuim*, 78 *M. gordonae*, 84 *M. kansasii*, 67 *M. scrofulaceum*, 15 *M. abscessus*, 3 *M. asiaticum*, 1 *M. flavescens*, 1 *M. gastri*, 52 *Mycobacterium* species, 4 *M. perigrinum*, 2 *M. shimodei*, 15 *M. terrae* complex, 9 *M. xenopi*, 18 *M. tuberculosis*.

Conclusion: 65% 1152/1759 of all positively identified isolates are the *M. avium intracellulare* complex (MAC) and 55% of these M. *intracellulare*. Previous studies have suggested that M. *intracellulare* is the more common pulmonary pathogen within the MAC. Therefore isolation of NTM is clinically relevant in Johannesburg and warrants further studies.

RISK FACTORS IN TUBERCULOSIS

PS-100607-14   An intervention to stop smoking among patients suspected of TB—preliminary results of a pilot RCT

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Introduction: In poorly resourced health systems which face a dual burden of disease secondary to tuberculosis and tobacco, an integrated approach to tackle tobacco dependence among TB suspects could be economically and practically desirable.

Objectives: To assess the incremental cost-effectiveness of a 'smoking cessation intervention package' to reduce tobacco dependence among TB suspects compared to usual care in Pakistan.

Methods: We designed an evidence-based treatment package based on WHO's 'five steps to quit' model. We planned a cluster RCT design and carried out a pilot trial first. The RCT consists of 3 trial arms: Control arm—Usual care + information leaflet; Intervention arm 1—Pharmacotherapy (Bupropion) + structured counseling + information leaflet; Intervention arm 2—Structured counseling + information leaflet. For the pilot trial, we recruited 150 patients (regular smokers) at six health facilities (two health facilities in each trial arm). The main outcomes to assess the effectiveness were point abstinence at 4 weeks and continuous abstinence up to 6 months.

Results: We present the preliminary results of our pilot trial. 67% of patients were found to be cigarette smokers ($n = 101$), while 12% ($n = 18$) smoke Huqqa and 15% ($n = 31$) smoke both Huqqa and cigarettes. The point abstinence at week 4 (validated by CO estimation) for the participants in the three arms shows that the in comparison to 40% (19/50) quit rates for the control arm, the quit rate for the intervention arm 1 was 36% (18/50) and that for the intervention arm 2 was 58% (29/50).

Conclusion: Our pilot helped us to refine our smoking cessation intervention package and mode of its delivery. The initial results, although not statistically

significant, are encouraging. We will now continue to carry out our cluster RCT in 33 health facilities in two districts.

PS-101034-14 Impact of smoking status and associated factors on tuberculosis treatment failure in Morocco

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Background: Tobacco smoking is a risk factor for tuberculosis (TB). However, the association between smoking and TB therapeutic failure has not yet been assessed in Morocco. The aim of this study is to evaluate the impact of smoking and associated factors on the failure rate of patients with TB.
Methods: Data from a randomized controlled trial conducted between 2004 and 2009 in 15 respiratory care units was examined to assess outcomes of TB treatment in relation to various risk factors. A total of 1039 new cases of tuberculosis (536 smokers and 503 non smokers) received treatment according to standard protocols and were followed up. Data about socio-demographic characteristics were collected by questionnaire. Treatment failure was defined as continued or recurrently positive cultures during the course of therapy. Univariate analyses were used to assess associations of treatment failure with smoking status, alcohol drinking and demographic characteristics. Multivariate logistic regression was used to adjust for potential confounding.
Results: Patients' mean age was 35.0 ± 13.2 years, 58.1% of patients were illiterate or had only basic education. Household monthly income was <2000 Dirhams (MAD)1 for 71.4% of patients. The rate of treatment failure was 6.9%. Failure was significantly higher among smokers (9.1% versus 4.5%; $P < 0.01$), those with less than 6 years' education (8.5% versus 4.5%; $P = 0.02$), people with a history of alcohol drinking (18.5% versus 4.9%; $P < 0.01$), and those with monthly income of <2000 MAD (8.4% vs. 3.3%; $P < 0.01$). There were no significant differences according to gender or age. After adjusting for confounding variables, smoking remained significantly associated with treatment failure; the adjusted odds ratio was 2.5 (95%CI 1.20–4.50), it was 3.5 of low income (95%CI 1.03–6.92).
Conclusion: Smoking is associated with TB treatment failure in Morocco. Antismoking Interventions are recommended to be included into current TB case management.

PS-101253-14 Evidence of benefits of an integrated tobacco cessation intervention in TB care on treatment outcome

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Background: There is unequivocal evidence supporting the association between tobacco smoking and tuberculosis (TB). Integrating TB and tobacco cessation interventions may produce significant benefits and is apparently logical. No study has extensively documented the evidence of clinical and humanistic benefits of such integration. A study from the context of a developing nation was conducted to determine this.
Methods: An intervention study was conducted at five chest clinics in Malaysia. Using a quasi-experimental design and the Transtheoretical Model approach, 120 patients who were current smokers at the time of TB diagnosis were assigned to either of two different intervention groups: TB-DOTS plus smoking cessation intervention (SCI) [integrated intervention group] or conventional TB-DOTS alone (control group). The impacts of the novel intervention on smoking cessation, TB treatment outcomes and health-related quality of life (HRQoL) were measured periodically.
Results: Smoking abstinence was biochemically validated using carbon monoxide and saliva cotinine testing. At the end of 6 months, patients who received the integrated intervention had significantly higher rate of success in quitting smoking when compared with those who received conventional TB treatment only (77.5% vs. 8.7%; $P < 0.001$). Furthermore, at 6 months or later, there were significantly higher rates of treatment default (15.2% vs. 2.5%; $P = 0.031$) and treatment failure (6.5% vs. 0%; $P = 0.031$) in the DOTS group than in the SCI-DOTS group. When compared, patients who received the integrated intervention had a better HRQoL (measured using EQ-5D questionnaire) than those who received conventional TB care (mean EQ-5D utility index = 0.98 ± 0.08 vs. 0.91 ± 0.14, $P = 0.006$).
Conclusion: This study provides evidence that an integrated TB-tobacco treatment is significant among patients who are smokers. The findings have important practice and policy implication in the revision of TB treatment guidelines.

PS-100420-14   Use of fluoroquinolone antibiotics leads to tuberculosis treatment delay in South African gold mines

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Background: Non-specific use of fluoroquinolone (FQ) antibiotics could delay TB treatment and give rise to FQ-resistant TB.
Methods: We examined the impact of FQ antibiotic use on TB outcomes, including smear status, treatment delay and FQ-resistance, by conducting a retrospective cohort study of 440 FQ-exposed and 511 non-exposed patients in a gold-mining community in South Africa. We considered both recent ($\leq$100 days before sputum collection) and distant exposure ($\leq$1 year). We determined FQ-resistance by the presence of gyrA mutations in 201 and 180 isolates from FQ-exposed and non-exposed individuals.
Results: Patients recently exposed to $\geq$5 days of FQ exposure were less likely to be smear positive (Odds Ratio [OR] = 0.27, 95%CI 0.11–0.63), with an increased time to treatment (time ratio [TR] = 2.02, 95%CI 1.19–3.44). The strength of association decreased when we included distant exposure. Controlling for smear status nullified the effect of FQ exposure on treatment delay. We detected a gyrA mutation in one isolate (0.5%) taken from an individual exposed to FQ for 8 days.
Conclusion: FQ exposure leads to treatment delay, an effect that is mediated by negative smear status. Short exposures to FQ do not routinely cause FQ resistance. Regardless, we recommend prudent use of FQ in settings of high HIV-TB burden.

PS-100810-14   TB is the leading cause of death from smoking in South Africa: results from 1 million deaths

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Indirect estimates of smoking attributable mortality derived from developed countries may be misleading if applied to low-middle income countries with different death profiles. South Africa included questions on smoking on the death notification form in 1997 to provide a more direct measure of tobacco attributed mortality. Of 4 million deaths between 1999 and 2006, about 1 million were 25 and 84 years and had all the relevant data. We used a case-control method to estimate relative risks of death from smoking and attributable fractions for major causes of death. 'Cases' comprised 497 380 people who died from causes related to smoking. Controls comprised 271 774 people who died of medical causes of death unrelated to smoking. The four major causes of death from smoking were: tuberculosis (OR = 1.3), cardiovascular diseases and stroke (OR = 1.2 to 1.6) COPD (OR = 2.2), and lung cancer (OR = 4.1), with 5052, 4435, 4125 and 2137 deaths, respectively, attributed to smoking. In all, smoking was responsible for at least 20 000 deaths in South Africa per annum, with a drop from 8% in 1998 to 5% of all deaths being attributed to smoking, primarily due to the rapid rise of deaths from HIV related conditions (primarily from tuberculosis) over this period. The leading cause of death from smoking is now tuberculosis (overtaking COPD-the leading cause in 1998), suggesting an important transition by both the smoking and the HIV related epidemics. The profile of deaths attributed to smoking in South Africa is thus still different from that observed in developed countries, and may evolve differently over time. The data were found to be generalisable and representative. Adding questions on smoking on the death notification form is a cost effective and accurate way to monitor smoking attributed mortality.

PS-100826-14   Comparison of risk factors for prevalent smear-positive and smear-negative TB

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Background: Risk factors for smear-positive (S+) and smear-negative (S−) TB disease may differ, but apart from HIV, there are few data directly evaluating this. We compared the effects of potential risk factors on S+ and S− TB.
Methods: Two TB prevalence surveys were conducted in separate random samples of adults aged $\geq$16 years, before and after the DETECTB cluster randomised trial of 2 TB case-finding strategies in Harare. Confirmed cases were classified as S+ or S− on the basis of 2 screening sputum specimens. Effects of potential risk factors on prevalent S+ and S− TB were estimated and compared using multinomial logistic regression.
Results: 21 303 adults participated in the two surveys combined; median age 27.9 years (IQR 21.9–37.2), 38% male, 20% HIV-infected. 65 (0.31%) S+

and 88 (0.41%) S– TB cases were diagnosed. The association between HIV and TB, observed among those without past TB treatment only, was stronger for S– (adj Risk Ratio 8.7, 95%CI 5.2–14.8) than S+ disease (3.8, 2.1–6.7; heterogeneity $P = 0.03$). The effect of past TB was similar for S+ and S– TB, and was apparent in HIV-negative participants only (RR 5.9 and 6.2, respectively). In contrast, household crowding was associated with S+ (RR for ≥ 2 persons-per-room 2.0, 1.2–3.5) but not S– TB (1.0, 0.7–1.6; heterogeneity $P = 0.05$). Smoking and household TB contact appeared more strongly associated with S+ than S– TB, though differences could be due to chance. Increasing age was associated with S– TB, but the trend was less consistent for S+ TB. Chronic cough was the strongest predictor of TB among various TB-related symptoms examined, but was substantially more predictive for S+ than for Sv disease in HIV-negatives or for either S+ or S– disease in HIV-positives.

Table Potential risk factors for prevalent smear-positive and smear-negative TB: multivariate analyses using multinomial logistic regression

Factors	Smear-positive TB		Smear-negative TB		Heterogeneity P value comparing RR's for smear-positive versus smear-negative TB*
	Risk ratio (95% CI)	P value	Risk ratio (95% CI)	P value	
Age (years)					
<25	1	0.043	1	0.055³	0.110
25–34	2.0 (1.0–4.0)		1.4 (0.7–2.7)		
35–44	2.0 (0.9–4.4)		2.1 (1.0–4.2)		
≥ 45	0.6 (0.2–1.9)		1.8 (0.8–3.8)		
Male	2.0 (1.1–3.6)	0.015	1.7 (1.1–2.8)	0.026	0.673
HIV infection					
Overall	3.3 (1.9–5.7)	<0.001	7.6 (4.6–12.5)	<0.001	0.027
Those without past TB treatment†	3.8 (2.1–6.7)		8.7 (5.2–14.8)		0.033
Those with past TB treatment†	1.0 (0.2–4.1)		1.7 (0.5–6.4)		0.594
Past TB treatment					
Overall	2.2 (1.0–4.8)	0.039	1.6 (0.8–3.0)	0.159	0.505
Among HIV-negatives†	5.9 (1.8–20.1)		6.2 (1.8–21.2)		0.955
Among HIV-positives†	1.6 (0.6–3.9)		1.2 (0.6–2.5)		0.656
Household TB contact in last 2 years	1.9 (1.1–3.5)	0.029	1.3 (0.7–2.3)	0.391	0.321
Household crowding ≥ 2 per room	2.0 (1.2–3.5)	0.010	1.0 (0.7–1.6)	0.951	0.046
Smoking					
Never smoked	1	0.071‡	1	0.345	0.516
<10 pack-years	1.3 (0.6–2.8)		0.8 (0.4–1.7)		
>10 pack-years	3.4 (1.1–10.5)		1.9 (0.7–5.0)		
Drinking ≥ 2 times per week	0.4 (0.1–1.1)	0.071	0.5 (0.2–1.2)	0.129	
SES index <25th centile§	0.9 (0.5–1.5)	0.652	0.9 (0.6–1.5)	0.799	0.861

* Assessed whether the effect of a given factor on smear-positive and smear-negative TB differ.
† P value for interaction between HIV status and past TB treatment was 0.086 for smear-positive TB and 0.024 for smear-negative TB.
‡ Test for trend.
§ A social economic index has estimated for each participants based on information regarding household assets using principal component analysis. This was then categorised according to $<$ or $\geq$25th centile for the overall distribution.

Conclusions: Potential differences in factors associated with transmission and pathogenesis of smear-positive and smear-negative TB could have important implications for TB case-finding and prevention strategies.

PS-100838-14   Prevalence of hepatitis C, hepatitis B and HIV co-infection among tuberculosis patients in Georgia

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Background: Georgia is country with high tuberculosis (TB), Hepatitis B virus (HBV) and Hepatitis C virus (HCV) prevalence. There are little data on rates of HCV and/or HBV co-infection among TB patients in Georgia.
Objectives: To determine the prevalence of human immunodeficiency virus (HIV), HBV, and HCV infections among patients with tuberculosis in Georgia and to determine the distribution and prevalence of HCV genotypes among persons with tuberculosis and HCV co-infection.
Design/methods: A prospective prevalence study was carried out from April 2007 to September 2009 at the National Center for Tuberculosis and Lung Diseases, Tbilisi, Georgia. Serological testing (ELISA) for HIV, HCV, and HBV serology and Versant HCV Genotype Assay (LiPA) for HCV genotyping were the diagnostic methods of the study.
Results: During the study period 346 newly diagnosed Tuberculosis patients were enrolled in the study. Serologic testing for HBV, HCV and HIV were available for 326 (94%) patients. Data analysis showed HCV prevalence to be 21% (68/326), HIV prevalence 1.5% (5/326) and HBV prevalence (by both HbsAg and/or HbcTotal) 33% (110/326). Hepatitis C virus genotyping results were available for 59 (87%) patients and determined the following types of HCV that are infecting TB patients in Georgia: type Ib in 21 (36%) TB cases, type 3a among 12 (22%) TB cases, type 2a/2c among 11 (18%) cases, type 2a in 2 (3%) cases. HCV genotype was undetectable for 12 (21%) TB patients and remained such for the two consecutive testing.
Conclusion: The study showed low prevalence of HIV among TB patients, but high prevalence of TB and Hepatitis C and B co-infection in Georgia. Taking into account that HCV is a major cause of chronic liver disease, further investigations need to be done to assess whether those persons with TB undergoing anti-TB treatment who have co-infection are at increased risk of developing drug induced hepatitis.

PS-100972-14 Risk factors of death from TB and other causes during one year after TB notification in Russia

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Background: Russia calculates tuberculosis (TB) mortality rate based on TB related deaths which were 58–59% of TB patients deaths happened in 2006–2008. Target impacts for prevention of TB patient death require evaluation of risk factors of TB patient death both from TB and other causes, as well as factors associated with a death happened during short time after TB notification.

Methods: Data of two groups of TB patients died in 2006 from TB (477 cases, 'T' group) and from other causes (286 cases, 'NT' group) in 3 Russian oblasts were analysed by univariable analysis and log-regression model to evaluate portion of deaths happened during year (DDY) after notification as a new TB case or relapse. Death certificates, autopsy protocols, and TB notification forms were evaluated and used also for validation of post-mortem diagnosis (TB or not TB) by four independent experts.

Results: Patients from T group more often then NT died during year after notification (62.7% and 52.8%, OR = 1.5, 95%CI 1.1–2.0). For T group DDY was associated with age >60 (OR = 1.9, 95%CI 1.1–3.3) and was prevented by 'working' and 'disabled' statuses (OR = 0.2, 95%CI 0.1–0.4) and OR = 0.4, 95%CI 0.2–0.8). While for NT group DDY was associated only with age <40 (OR = 2.7, 95%CI 1.5–4.9). Significant exceeding of portions of TB patients who DDY in T group vs. NT were found for age older 40, female and not alcohol-abused (OR = 2.6, 95%CI 1.8–3.7; OR = 2.4, 95%CI 1.1–5.3; OR = 1.4, 95%CI 1.02–2.0), opposite result was for working TB patients (OR = 0.3, 95%CI 0.1–0.9). Data validation has shown 2.2% disagreement with 'TB' and 3.9% with 'non TB' diagnoses as deaths causes.

Conclusion: Reduction of level of a TB patients' mortality, especially DDY, demands improvement of case-finding and etiotropic therapy, as well as effective treatment of concomitant diseases and social support of vulnerable patients which are significant portion of TB patients. Studied regions had satisfactory quality of post-mortem diagnostics TB as a cause of death.

PS-101380-14 Tuberculosis stigmatization is associated with disease concealment and poor treatment adherence

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Background: TB related stigma has been implicated in delayed testing, treatment intermittency and default, which increase the risk of secondary transmission and development of multidrug-resistant TB (MDR-TB). The objective of this study was to assess TB stigma as a possible mediator of poor treatment adherence in the high TB incidence shantytowns surrounding Lima, Peru.

Methods: This cohort study involved 2176 residents in TB-affected households: TB patients ($n = 710$) and their healthy household contacts ($n = 1466$) in 16 adjacent peri-urban shantytowns in Lima/Callao, Peru. Participants were interviewed in the final month of TB treatment. The survey instrument comprised of 22 questions concerning experiences of TB-related stigma in three domains: home, community and work. Principal component analysis was used to develop a stigma score. Poor adherence was defined as default or intermittent TB treatment.

Results: Experience of stigma was endemic among TB affected families (83% of patients and 77% of household contacts). Among patients, increased stigma in the home and community were associated with factors such as female gender (OR = 2.0; $P = 0.03$), lower income (OR = 3.8; $P = 0.01$), previous TB (OR = 1.7; $P < 0.01$), and MDR-TB (OR = 2.4; $P = 0.03$). In turn, stigma in the home and community was a risk factor for poor treatment adherence
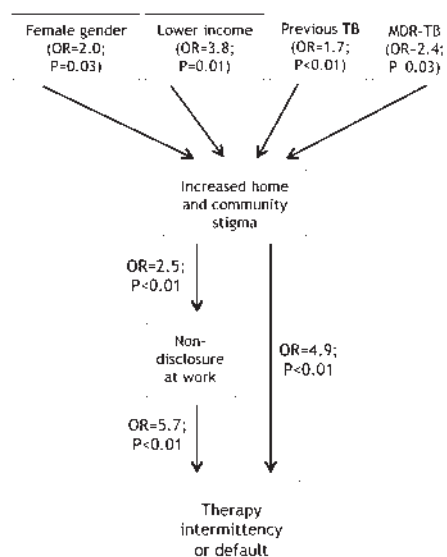
along two pathways: either as a direct risk factor (OR = 4.9; P = 0.01), or indirectly through the mediation of TB concealment at work (OR = 2.5; $P <$ 0.01), which was found to be the strongest predictor of poor adherence in the study population (OR = 5.7; $P <$ 0.01). The pathway for this relationship is shown in the figure.

Conclusions: TB patients who suffered stigmatization at home and in the community were more likely to keep TB a secret at work, and were at significantly greater risk of poor treatment adherence. Risk of poor adherence due to stigmatization in this context is substantial, and should be targeted in intervention strategies.

PS-101417-14 To screen or not to screen: a systematic review of screening studies on tuberculosis and diabetes

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Background: Diabetes mellitus (DM) is increasing in areas of high TB burden. Screening may be an effective strategy for tackling the dual burden.
Objective: To consider the utility of screening diabetics for TB and of screening TB patients for the presence of DM through a systematic review of published studies.
Methods: We performed a systematic search for screening studies in diabetics or TB patients in PubMed and EMBASE. Studies were included if they 1) reported the number of TB cases identified among diabetics, or 2) reported the number of DM cases identified among TB patients. We computed prevalence ratios and prevalence difference to compare yield of screening for TB in diabetic populations to that in non-diabetic controls or the general population, and to compare the yield of screening for DM in TB patients to that in non-TB controls or the general population. We computed the number of people to screen to detect 1 additional case of TB or DM by taking the inverse of the prevalence difference.
Results: TB prevalence ratios ranged from 2 to 5 in five studies that screened for TB in diabetics. TB prevalence was higher in insulin-dependent diabetics than in those not requiring insulin. Based on the computed prevalence ratios, the number of diabetics to screen to detect 1 additional TB case would range from 50 to 200 in areas of high TB prevalence (500/100 000). DM prevalence ratios ranged from 1.8 to 8 in seven studies that screened for DM in TB patients. Based on these ratios, the number of TB patients to screen to detect 1 additional case of DM would range from 3 to 25 in an area of 5% DM prevalence.
Conclusion: We recommend screening for TB in dia-

betics in places of high TB prevalence, especially among insulin-dependent diabetics. DM should be screened for and monitored in TB patients of any setting.

PS-100795-14 The relationship between tuberculosis burden and poverty in Taiwan

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Background and Objective: The per capital gross domestic product (GDP) in Taiwan since year 2004 has been higher than US$14 000 and classified as a high-income country. Despite of economics growth, in year 2009, 1.11% of households came from low-income families. In mountainous areas, the average incidence of TB was 3 times higher than the general populations in Taiwan. The aim of this study was to understand the link between TB and poverty, and to develop the strategy of better TB control.
Materials and methods: Data of TB notification rates of 25 cities/counties from CDC national surveillance registry and income information from the statistical yearbook from Ministry of the Interior during the period of year 2005 to 2008 were analyzed. Correlation and regression analysis were applied to explore the correlation between the TB incidence rate and the proportion of low-income families.
Results: The 25 sets of average data of TB incidence and low-income rate during year 2005–2008 were compared. The higher the low income rate, the higher the TB incidence rate was and the correlation was statistically significant (R2 = 13.7%, $P <$ 0.05). Accompanied with mountainous villages, ranking of low income rate had high explanation power (R2 = 47.1%, $P <$ 0.05) and both of these two factors influenced TB incidences significantly in the multiple regression model.

Table Analysis of ranks of mountainous villages, low income rates and TB burden by multiple regression analysis (N = 100)

Variable	Parameter estimate	Standard error	T	P value	95% CI
Intercept	47.753	3.181	15.014	0.000**	41.440~54.065
Mountainous villages	7.616	0.949	8.024	0.000**	5.732~9.500
The ranking of low income rate	6.362	1.755	3.625	0.000**	2.879~9.845

**$P <$ 0.001.

Conclusion: These findings highlight the linkage of proportion of low-income families with the burden of TB in Taiwan. Appropriate, free, and active TB screen services and integrated resources from social assistance system and medical-public health system should be provided to low-income families.

PS-101093-14   Tuberculosis and waterpipe smoking: any association or increased risk?

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Aim: To explore the relationship of waterpipe smoking to tuberculosis infection and compare it to cigarette smoking. Sharing waterpipe is common among users and although it seemed logical that this may lead to increased transmission of tuberculosis, this has not been studied before.

Design/methods: A case control study was designed including all newly diagnosed pulmonary tuberculosis cases over 6 months in all treatment facilities of the ministry of health in Egypt. Two controls of same gender and 5-years age group were selected from nearby ministry facilities for certifying food handlers or outpatient clinic attendants (not related to chest disease). Verification of Non-TB status was done using a health questionnaire of suggestive symptoms and when clinically required, X-ray chest and sputum testing. All subjects were interviewed for tobacco smoking (waterpipe or cigarettes). Statistical comparisons were performed to examine the odds of waterpipe smoking among TB cases compared to non users of tobacco and to cigarette smokers.

Results: 995 cases and 2000 control are enrolled so far in the study. Ever smoking was reported by 67% of TB male cases versus 50% of control males with an odds ratio (95% confidence limits) of 2.1 (1.7–2.5) while among females ever smoking was reported by 3% versus 3.8% among controls ($P > 0.05$). Daily waterpipe smoking was reported by 19.0% of male cases versus 11.4 among control (OR 1.9, 95%CL 1.3–2.6), while daily cigarette smoking was reported by 61% vs. 41% (OR 2.3, 95%CL 1.9–2.8). Sharing waterpipe was not statistically different between cases and controls.

Conclusion and recommendations: This study shows for the first time that water pipe smoking is associated with an increased risk of tuberculosis of nearly similar magnitude to that of cigarette smoking. Further testing of the waterpipe equipment of TB cases for DNA of TB bacilli is underway.

PS-101458-14   Determinants of smoking among male patients with pulmonary tuberculosis (ETTAM study)

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Background: Tobacco smoking and lung tuberculosis (TB) represent a health problem in Morocco. The aim of this study was to estimate associate factors of current smoking among Moroccans males with lung tuberculosis.

Methods: We used a data from a randomized controlled trial conducted between 2004 and 2009 in 15 respiratory care units. A total of 596 new cases of lung tuberculosis (332 non smokers and 264 current smokers) received treatment according to standard protocols and were followed up. Data about sociodemographic and smoking behaviors characteristics were collected by questionnaire. Univariate analysis was used to assess associations of smoking status and characteristic of population.

Results: 26.6% of smokers started smoking before the age of 15 years, 54.4% between 16 and 20 years. Among smokers, 45.3% smoked 10 to 20 cigarettes per day, 58.6% spend between 10 and 20 Dh* per day for their smoking, 32.5% have never tried to quit smoking and 52.8% had tried up to three time, 59.6% of smokers light their cigarettes in 30 minutes after waking. 57.2% of smokers were aged under 30 and 50.3% of non-smokers were aged between 30 and 40 years ($P < 0.001$). 49.9% of non-smokers and 38.6% of smokers had a higher educational level ($P < 0.01$). 30.2% of smokers and 33.3% of non-smokers had a professional activity. 81.8% of smokers and 75.9% of non-smokers were of urban origin. 61.1% of non-smokers and 33.3% of smokers were practicing Muslims ($P < 0.001$). 19.6% of smokers and 1.2% of non smokers are drinkers ($P < 0.001$). 51.0% of smokers and 28.3% of non-smokers were exposed to tobacco in their family environment ($P < 0.001$). 68.8% of smokers and 56.8% of non-smokers were exposed to tobacco in their professional environment ($P < 0.01$).

Conclusion: This study provides baseline data for antismoking interventions for males with lung tuberculosis.

*1 Euro = 11 Dh.

PS-101036-14   Double trouble: diabetes and tuberculosis in a Pacific Island

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Background: Westernization of the local diet has caused marked increases in BMI and led to extremely high rates of diabetes in the Pacific. In the CNMI, a small US-Associated Pacific jurisdiction, the diabetes rate for adults is 28%. Because diabetes is an important risk factor for development of tuberculosis, the prevalence of diabetes in TB patients across the Pacific is also very high. Several program changes are indicated to improve diagnosis and treatment of TB cases amongst patients with coexistent diabetes.

Intervention: The CNMI TB Control Program reviewed the prevalence of diabetes amongst TB cases over the past 6 years. Remarkably, the rate of diabetes amongst adult Pacific Islanders exceeded 70%. Literature investigating the link between these diseases was reviewed, with a focus on achievable program interventions to improve patient management for diabetics with tuberculosis.

Results: The CNMI TB Control Program created local guidelines to improve the management of TB patients with diabetes. Several program changes include: mandatory diabetes screening for all adult TB cases, special attention to potential interactions between medications, and extending the treatment course to 9 months in many cases. Most prominently, the program cross-trained DOT staff to provide simple diabetes education as an integral part of DOT for these patients.
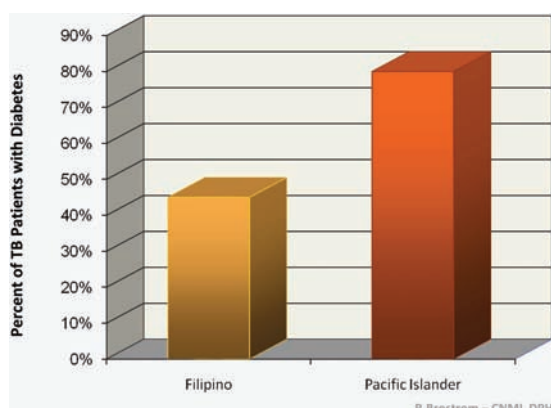
Figure TB and DM in CNMI: 2005 & 2008 (Age > 25, *n* = 175).

Conclusions and key recommendations: Marked increases in diabetes rates across the world, particularly in places where TB rates are already high, may lead to an increased burden of TB disease in many regions. CNMI recognized the need to adjust the TB Control program with simple guidelines to improve the TB care delivered to diabetic patients. Several achievable TB program changes can help to address the many complications of treating patients caught in the cross-fire between tuberculosis and diabetes.

PS-100947-14   Promoting TB and tobacco work at country level

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The confirmed causal associations between tobacco use and TB outcomes should become the basis of joint efforts to tackle the dual epidemics. Since 2005, WHO Tobacco Free Initiative (TFI), the WHO Stop TB! Department (STB) and the International Union Against Tuberculosis and Lung Diseases (The Union) have been exploring collaborative activities between TB control and tobacco control efforts and the WHO/The Union recommendations for controlling the two global epidemics have been developed and piloted. The next step is to increase political awareness and commitment to implement the recommendations at country level, which can learn from the success of the joint TB-HIV efforts. The key activities will include: 1) Raising a higher profile for TB and tobacco work at country level; 2) Reviewing country experience on integration of TB and tobacco control interventions; 3) Learning from the success of the joint HIV-TB efforts to address TB and tobacco; and 4) promoting the implementation of the WHO/The Union recommendations on TB and tobacco control at country level.

TB CASE DETECTION: DELAYS/ COST EFFECTIVENESS/HEALTH SEEKING BEHAVIOURS

PS-101418-14   Access to the diagnosis of tuberculosis in health services in the municipality of Vitória, ES, Brazil

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Introduction: In Brazil, since 2004 primary health attention is adopted for actions on tuberculosis control.

Objective: To evaluate the access to the diagnosis of tuberculosis (TB) in Vitória, Espírito Santo.

Methods: A cross sectional study utilizing the Primary Care Assessment Tool (PCAT) instrument was used. A convenience sample that was composed of patients in TB treatment who reside in Vitória, with age equal to or greater than 18 years old and were diagnosed between January and December of 2009.

The data was collected by a semi-structured interview and secondary sources of information (patient forms). The data analysis was made by descriptive statistics techniques.

Results: From the 101 patients interviewed, there was a predominance of the male gender (59.4%), incomplete basic education (55.4%) and resided in their own houses (93%). With relation to the entry door, it was observed that, although the majority of the patients sought care at a primary care unit (30.7%), the diagnosis in the Tuberculosis Control Program predominated (56.4%). A few patients were diagnosed at private health services (1%). There was a greater prevalence of the characteristics that show lower social-economic conditions.

Conclusion: It was concluded that a great part of the diagnosis of TB was made at secondary levels of attention, while basic attention was not as representative in the diagnosis process, which conferred upon Vitória peculiarities that should be considered in face of implementation actions for the diagnosis of TB in the municipality and in the elaboration of public health policies.
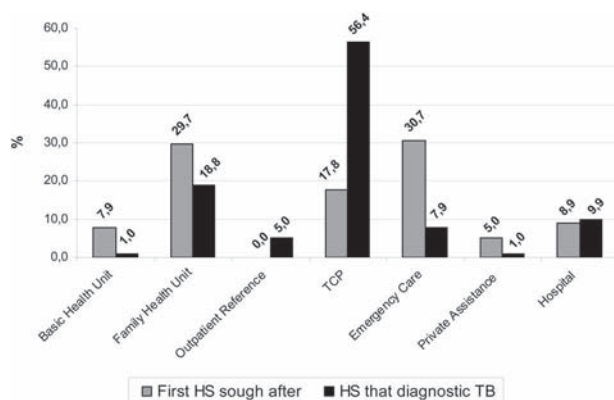

Figure Frequency distribution of the types of health services that diagnosed TB and the first health service sought after by patients in the municipality of Vitória, ES, 2009. TCP = Tuberculosis Control Program; HS = Health Service.

PS-100095-14 Patient and health system delay for tuberculosis diagnosis in Brazil

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Aim: The delay in diagnosis of pulmonary TB is an important aspect in the chain of transmission, and may also result in advanced disease and in financial burden for the patient and the health system. Among other strategies, the STOP-TB recommends DOTS implementation and expansion, which should result in increased access and rapid diagnosis of TB. In this study, we evaluated the time spent since the patient noticed the onset of symptoms until he/she searched for medical help (patient delay), and the delay for the diagnosis to be made (health system delay).

Methods: Previously trained medical students interviewed patients with active pulmonary TB between the 4th and the 12th week of treatment in two Brazilian cities. A total of 166 patients were interviewed, 64 in Belém, and 102 in Curitiba. Duration of symptoms before search for help and from this moment to diagnosis were analyzed.

Results: The Table summarizes the results. Median patient delay was 34 days in Belém and 53 in Curitiba. System delay was 28 days in Curitiba and 12 days in Belém. In both cities, patient delay accounted for most the delay in diagnosis.

Conclusion: Diagnosis of TB is delayed, mostly because of patients delay in seeking for help. Despite free access to dispensaries with diagnostic means, patients still go to emergencies or pharmacies before looking for primary care units. Advanced disease may be a reason for looking for hospitals. Self-medication is a special problem. Multiple visits and need for hospitalization may result in financial burden for the patient and for the healthcare system. Community empowerment is an important aspect in achieving shorted patient and health system delay in TB diagnosis.

Table Patient and health system delay for TB diagnosis in Belém and Curitiba, Brazil

	Belém $(n = 64)$ Median (IQR)	Curitiba $(n = 102)$ Median (IQR)
Patient delay (days)	34 (30–109)	53 (21–90)
$\geq$60 days	47%	52%
System delay (days)	12 (0–52)	28 (11–66)
$\geq$30 days	38%	47%
Total delay (days)	87 (38–155)	82 (36–169)

PS-101358-14 Former TB patient volunteers contribute to intensified TB case finding and community awareness on TB

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Background: MUKIKUTE is a Tanzanian NGO composed of former TB patients. In collaboration with the Ministry of Health, MUKIKUTE facilitates the establishment of TB clubs, provides TB-HIV education at community level, directly supervises TB patients' TB treatment, and orients traditional healers

to identify TB suspects and to refer them to the health facility. To date, MUKIKUTE operates at a national level through 20 TB clubs in 8 regions.

Results: In 2009 a 3-day orientation was conducted with 320 TB patients in Dar es Salaam region to teach them skills in educating the general population on TB-HIV and eventually become treatment supporters to other TB patients. After training, 80 MUKIKUTE former TB patients oriented over 6500 people at community level in 2 districts of 2 regions (Dar es Salaam and Pwani); 601 TB suspects were identified through active case finding at community level and referred to the health facility and among them, 43 TB cases were identified. Community leaders ($n = 480$) and influential people were sensitized on TB-HIV during a 1-day orientation in 1 district of Dar es Salaam region; 40 traditional healers received one day orientation on TB-HIV and referral of TB suspects to the health facility. MUKIKUTE volunteers directly supervised TB treatment of 168 TB patients until their treatment was successfully completed. They also successfully traced TB patient defaulters notified by the MOH.

Conclusions: About 9% of those reached through community sensitization and active case finding of MUKIKUTE volunteers were TB suspects, and 7% of TB suspects were diagnosed with TB. Two-thirds (66%) of registered traditional healers in target areas were oriented on TB control. Volunteers demonstrated high success rates in DOTS support and defaulter tracing. Recent partnership with ICAP-Columbia University will provide MUKIKUTE with additional support to expand TB clubs and increase TB case finding.

PS-100566-14 Mobilizing poor migrants to access free early TB detection and treatment

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Aim: To assist poor migrants access early tuberculosis (TB) diagnosis and treatment in poor resource and hard to reach setting.

Background: International Organization for Migration (IOM) has a registered free directly observed therapy (DOT) TB clinic in poor Nairobi suburb—Eastleigh with a high population of both registered and unregistered migrants. This suburb is known to have high incidence of TB. Unregistered migrants have difficulty in accessing healthcare due to fear of arrest; however, IOM deals with all migrants irrespective of their legal status.

Method: IOM mobilized the community through posters, visits to mosques, meeting with community leaders to sensitize them on available free TB screening and treatment. In this regard anyone with known believed or suspected TB symptoms and signs is welcome to the IOM TB clinic. In 2009, 342 clients were

tested for TB by sputum smear microscopy of which 212 were migrants. Of the 212, 42 (19.8%) had at least one positive smear. All positive samples had TB culture and drug susceptibility testing (DST) done, in all cases *Mycobacterium tuberculosis* was isolated. 40 were pan-susceptible to tested 1st line anti-TB drugs while one had streptomycin resistance and one had multidrug resistance (MDR) TB. All 42 received appropriate DOT anti-TB therapy.

Conclusion: We can use very limited resources to achieve high rate of early TB detection in hard to reach population within already established TB centres. Community acceptance/trust of IOM as the care giver greatly contributed to the success of this objective.

PS-100804-14 Challenges in implementing the out-reach X-ray service within the urban community in Zambia

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Background: Chest X-ray (CXR) is necessary for the diagnosis of smear-negative patients in the high prevalent HIV setting. However, the accessibility to CXR facility is still limited in Zambia, which may cause diagnostic delay. The road conditions often make it difficult to utilize the mobile X-ray car in the community.

Intervention: The project set up the TB diagnostic center where sputum AFB, culture, HIV test and CXR are available in Bauleni, an urban community in Lusaka with 65 000 population. The accessibility to TB diagnosis of this area was not well established. The first challenge we faced was to find an appropriate structure for the services. Secondly, the renovations were required for the radiation protection such as Barium plaster application on the wall and lead doors, also for the dark room in accordance with the Zambian regulations. Thirdly, the power generator had to be installed due to unstable power supply. At the center, the sputum samples are collected and sent to a referral TB laboratory for AFB and culture whereas CXR and HIV rapid test are done on site. Once TB diagnosis is done, the patients are referred to the government health facility within the community for the treatment.

Results and lessons learnt: Since August 2009, the center has received 498 TB suspects and 212 have been diagnosed as TB. Among 212, 64 (30.2%) were diagnosed by smear, 9 (4.2%) by culture and 139 (65.6%) by CXR; 207 (97.6%) are HIV status known and 133 (62.7%) are HIV positive. Among 139 X-ray diagnosed cases, 45 (32.4%) have been confirmed by

culture later. X-ray was also useful to diagnose 46 extra-pulmonary TB cases with legions in chest area such as pleuritis or pericarditis.

Conclusions and recommendations: Despite all the challenges mentioned above, out-reach CXR service has contributed to intensified TB case finding in HIV high prevalence setting like Zambia.

PS-101108-14   Access to routine clinic compared to community sputum collection for tuberculosis diagnosis

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Introduction: Identification of prevalent smear positive tuberculosis (TB) is a global priority. Enhanced case finding (ECF) for TB is an innovative modality incorporated into the Zambia South Africa TB and AIDS Reduction study (ZAMSTAR).

Aim: We hypothesized that the demographics of individuals accessing ECF as opposed to routine TB diagnostic services in four communities in the Western Cape, South Africa would be different.

Methods: ECF activities included drama performances, educational activities and fast track sputum collection systems in communities and routine healthcare clinics. Details of TB suspects over 18 years of age were recorded in Sputum Registers from October 2006 to September 2009. Sputum registers were manually compiled and then captured electronically.

Results: Of the 17 846 people accessing routine clinic services there were 52.1% males ($n = 9295$), 47.9% females ($n = 8551$) and the mean age was 36.83 years. Of 4807 people accessing ECF there were 53.7% males ($n = 2582$), 46.3% females ($n = 2225$) and the mean age was 37.62 years. There was a statistical difference in age ($P = 0.0008$) and gender ($P = 0.045$) between the two groups.

Conclusion: Although there was a statistical difference in the demographics of the two groups, this did not translate into a clinically significant difference. ECF, which was expected to attract a younger age group through its use of educational drama performances and easy access community sputum collection points, essentially targeted individuals with similar age and gender as those who access existing routine clinic diagnostic services.

PS-100802-14   Increasing case detection in low performing areas of Bangladesh: experience in a FIDELIS project

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Background: BRAC, an NGO in Bangladesh working in collaboration with NTP has an average detection rate above 70%. However there are still small pockets with lower case detection rate. BRAC undertook a FIDELIS project in October, 2008 targeting 84 sub districts whose case detection rate below 70% covering total 27.4 million population.

Objective: To increase case detection rate of new smear positive cases from 54% (55 per 100 000) to 70% (72 per 100 000) and to treat successfully 91% of the detected cases.

Intervention: Additional measures included school students and community leaders' orientation. Incentive was provided for decentralized sputum collection centers organized in remote areas. Messages on TB disseminated through cable television and miking, drum beating in community. Posters & leaflets were developed in indigenous languages.

Results: From October 2008 to December 2009, total 87 309 school students, 2124 traditional leaders were oriented and 1202 miking and 6376 drum beating events were organized. Total 23 818 NSP cases were diagnosed and case detection was 69.4% (71 per 100 000). Treatment success rate up to December, 2009 was 93%. By December 2009, total 34 sub districts could reach above 70%. Those who could not reach, most of them had a lower baseline of less than 50% initially. Some were also very hard to reach or of urban characteristics.

Conclusion: Special interventions are needed to be continued for area with low detection rate. Further exploration of the specific factors behind the low detection rate could be assessed to strengthen the interventions.

PS-100856-14   The role of TB diagnostic committee in certifying disease activity among smear-negative PTB cases

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Background: The TBDC is a committee that decides on the presence or absence of disease activity among symptomatic and asymptomatic patients with lesions suggestive of TB on their chest radiographs and whose sputum AFB smears are negative.

Objectives: To describe the TBDC experience in District IV of Manila, Philippines from 2007–2008.

Methods: All cases seen by TBDC District IV from January 2007 to December 2008 were included in the study. The summary of report for each meeting

was tabulated and descriptive statistics was done using SPSS version 14.

Results: A total of 653 cases were referred to TBDC District IV in the study period. In 2007, 43.1% (116 out of 269) were decided upon by the TBDC as inactive and therefore not warranting treatment during the time of referral; while in 2008, a higher rate of 58.9% (226 out of 384) did not warrant treatment. There were 56.88% (153 out of 269) of cases who was decided to be given treatment in 2007 while 41.15% (158 out of 384) of cases were recommended for anti-TB treatment in 2008. There were a total of 158 (55 in 2007; 103 in 2008) chest radiographs evaluated to be of poor quality.

Conclusion: The TBDC of District IV was able to detect 47.6% of smear negative patients to be recommended for treatment in the year 2007–2008. Poor quality chest X-ray was encountered in 158 cases during the study period. TBDC is an approach that can be replicated in other high burden TB countries, which may reduce the level of over-diagnosis and over-treatment among smear-negative PTB cases. It likewise is an opportunity to check the quality of chest X-ray facilities and possibly regulate their licensing.

PS-101316-14   Community contribution in TB case detection: experience from Malawi

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Background: The Malawi National TB control Program (NTP) developed a universal access strategy to TB diagnosis and treatment in 2007 aimed at implementing various initiatives to improve TB case detection targeting health facilities and communities. TB-CAP supported the NTP in implementing this strategy in Zomba and Mangochi districts. We assessed the contribution of community initiatives in TB case detection in two years of implementation.

Methods: Community Based Organizations (CBO) and Village Health Committees (VHC) which previously provided HIV/AIDS services were supported to integrate TB into their activities. These were given material and capacity building support and have since established 187 community sputum collection points (SCP). Apart from collecting and transporting sputum specimens to microscopy centers, the CBOs and VHCs also promote compliance to TB treatment, screen for TB among PLHIV, conduct advocacy and community awareness campaigns.

Results: Community initiatives contributed 14% (3277/23758) of TB suspects and 15% (285/1881) of smear positive TB patients diagnosed in the two districts in 2008/2009. The graph below, shows number

of TB suspects steadily increased while the smear positivity rate remained constant before and after the introduction of community initiatives.
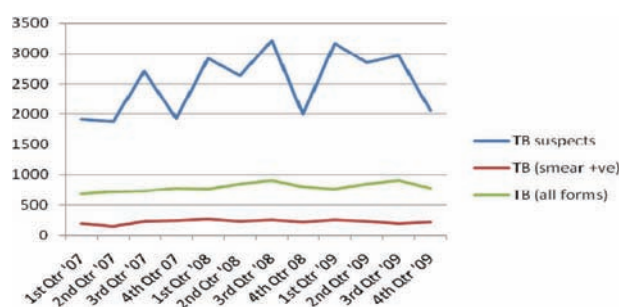
Figure   Trend of TB in Mangochi and Zomba.

Conclusion and recommendations: Community initiates have significantly contributed to improving TB case detection. Efforts should be made to strengthen the capacity of VHCs and CBOs and improve the quality of sputum specimens. The initiative should be scaled-up.

PS-100913-14   Factors of delay for tuberculosis diagnosis and treatment in the Province of Luanda, Angola

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Aim: A high rate of treatment interruption (67%) and a low rate of treatment success (29%) have been documented until 2006 in the Province of Luanda, Angola. In the frame of a study aimed at improving the National TB Programme, we have investigated the factors influencing the days (d) of delay in TB diagnosis over a cohort of pts referring to the TB DOT clinics in the Province of Luanda.

Methods: Structured questionnaires were randomly administered to a representative sample of TB pts. Three types of delays were identified and defined: A) Patient-related delay (period of time from symptom onset to the 1st visit), B) System-related delay (from the 1st visit to the initiation of TB therapy), and C) Total delay. Globally, reasonably acceptable thresholds for delay are 30, 15 and 60 d for type A, B, and C, respectively. The means of delay have been stratified by sex, positive or negative sputum, level of education and health facility at the first visit, and assessed by univariate analysis.

Results: 385 pts have been interviewed. The means of delays were 71, 28 and 100 d for type A, B and C, respectively. Type A delay was found to be significantly ($P < 0.05$) higher than type B. The type A and B delays were observed to be lower ($P < 0.05$) in males and in pts who had undergone the 1st visit at

DOT clinic compared to non-DOT clinic either public or private (OR 041, 95%CI 0.26–0.67, *P* < 0.01). **Conclusions:** The mean delays were higher than expected, and significantly associated to patient delay. First visit not at the DOT clinic and female sex were found to be significant risk factors for increased delay. Pt delay is the result of multiple factors that precede the contact between pt and health facility. Since prompt diagnosis and treatment are elements than can affect the indicators of TB programmes, strategies aimed at reinforcing the role of DOT clinic at community level are expected to decrease the delay between symptom onset and first contact with the health facility.

PS-100996-14   Cost-effectiveness of enhanced TB case-finding in South Kivu, DR Congo: a comparative analysis

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Rationale: TB case finding in South Kivu remains steady below national level. Major obstacles to health services utilization are financial and social. Since 2007, two interventions were piloted in addition to self-reporting: Intervention A is economic and targets both supply and demand; it comprises of third-party financing of subsidized services including consultation and hospital admission, with a performance based share. TB is included in the package. Intervention B is social and targets demand; it comprises of active case finding and psychosocial support by an organization of ex-TB patients. We evaluate the potential of these strategies compared to classic DOTS from the point of view of effectiveness and cost-effectiveness.
Methods: Retrospective evaluation through:
—Comparison of Sm+TB case detection between 2005 and 2008
—Cost/effectiveness analysis based on 2008 expenditure
Results: The number of Sm+ new cases detected increased from 57 in 2005 to 231 in 2008 (451%) under Intervention A, and from 275 in 2005 to 400 in 2008 (145%) under Intervention B. In areas with no intervention, it decreased from 1964 in 2005 to 1851 in 2008 (−6%). Total cost was $17 235 and $22 350 where Interventions A and B respectively were implemented, and $92 550 elsewhere. The cost-effectiveness of Interventions A, B, and regular NTP operation was 65, 56 and 50, respectively. Sensitivity analysis confirms the trend.
Conclusion: Interventions targeted at removing social and economic barriers improve case detection when passive case finding has reached a steady state. Economic barriers seem higher than social ones when full cost recovery is the rule for health services in areas of high poverty. Despite higher cost/effectiveness, investing in enhanced case finding appears justified as a marginal cost to achieve TB control objectives. Improving health financing addressing both patients and health workers constraints is a priority in reconstructing DR Congo health system.

PS-100898-14   The role and cost-effectiveness of a special medical commission in diagnosis of sputum smear-negative tuberculosis

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Background: Study of the epidemiologic data from TB facilities in Tbilisi for 2002–2005 showed that the registered sputum smear-negative (SS−) pulmonary TB (PTB) cases decreased from 77.9% to 54.5%. Despite this the share of PTB (SS−) cases still remained high. Therefore it was reasonable to establish special medical commission (MC) responsibility of which was to study and to make diagnosis of every suspicious PTB SS− case identified in the TB networks.
Aim: Assessment of the special MC role in improvement of TB diagnosis quality and calculation of the medical examinations costs of PTB (SS−) diagnosis at out- and in-patient facilities in order to identify the most cost-effective project.
Methods: Medical examination on the outpatient level included blood count, AFB identification tests and chest X-ray carried out before and after chemotherapy with the antibiotics of wide range of action. At inpatient level for 4-day medical examination lung CT, cytologycal and bacteriogical test of biopsy material after bronchoscopy was added.
Results: In 2008 there were registered 1336 PTB cases in Tbilisi. 818 (61.3%) of them were SS+ and 518 (38.8%) SS−. The most PTB (SS−) cases were detected in the 21–30 age group (29.9%). Culture was performed in 344 cases. The growth of the culture took place in 228 cases (66.3%). In smear negative and culture positive cases 170 (74.6%) were new and 58 (72.2%) previously treated cases. 374 (72.2%) cases were diagnosed by MC and 144 (27.8%) by consultation of doctors after 4-days course of medical examinations. Costs of out-patient medical examinations per patient made up 70 GEL (40.46 USD), while the cost of 4 days clinical investigations at inpatient level was 685 GEL (395.95 USD).
Conclusions: The results of the study made obvious the significant role of MC in improving the quality and cost-effectiveness of the TB case detection.

PS-100836-14   Recapturing the registered TB patients and active TB case finding among IDPs in NWFP, Pakistan

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Background: In the year 2009 North West Frontier Province of Pakistan witnessed worsening security situation which resulted in displacement of around 4 million people from the districts of Swat, Buner and Lower Dir to the neighboring districts. The TB Control programme NWFP decided to intervene in order to prevent the treatment interruption for already registered TB patients (prior to displacement the programme had registered 1658 patients during the Q4 2008 and Q1 2009 in the three districts) and to go for active case finding in the overcrowded IDP populations.
Interventions: The programme strategy was based on the following interventions in the neighboring 5 districts: 1) Forging partnerships; 2) Human resource strengthening; 3) Establishing diagnostic channels; 4) Ensuring uninterrupted drugs supply; 5) ACSM campaigns; 6) Recording and reporting; 7) Monitoring and supervision.
Results and lessons learnt: A total number of 973 TB cases in continuation phase of treatment were recaptured and continued on treatment. Of the total 973 cases in continuation phase 758 (77.9%) were recaptured in the first month of the mass displacement. Most of the patients proactively approached the health facilities and demanded for continuation of their treatment. This is attributed to effective induction counseling of patients at the start of the treatment. 400 new TB cases were detected and registered among the IDP population.

Table   Total No of TB cases in IDPs

District	Continuation phase	New cases	Total
Mardan	505	150	655
Nowshera	123	88	211
Swabi	119	32	151
Charsadda	157	77	234
Peshawar	69	53	122
Total	973	400	1373

Conclusion and key recommendation: Timely programme interventions in mass immigration situation prevent the interruption of TB treatment. Effective induction counseling of TB patients is important in motivating them to complete the treatment. Active case finding in these situations prevents diagnostic delay and facilitates early case detection.

PS-101169-14   Active search of respiratory symptoms in tuberculosis control in the indigenous population, Brazil

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Background: Tuberculosis (TB) is an important morbidity and mortality factor among the indigenous populations of Brazil, and the incidence rates are alarming the competent health authorities.
Aim: It was aimed to identify the problems related to the active search of Respiratory Symptoms (RS) in TB control in the indigenous communities of Paraiba-Brazil.
Methods: Qualitative research that used the Focal Group technique with three indigenous health teams of the Special Indigenous District in the state of Paraiba-Brazil. The empiric material obtained was analyzed by the critic approach of the Speech Analysis technique.
Results: It was evidenced that the actions of search of RS did not correspond, in practice to a service routine, basing on punctual and restrict actions to mobilizations in the Epidemiologic Surveillance Sector that in partnership with the teams make use of elements not incorporated to the protocol of search of RS, with the example of formularies. It was observed the lack of structure of the local service as for the availability of inputs, lack of accountability of the team in the organization of the flow of material for bacteriological exam and difficulties in the approach of the patient in the moment of the sputum collection.
Conclusions: It was concluded that the active search for RS by the indigenous health teams is permeated by limitations that difficult the decentralization of these activities for the basic health units and the incorporation of these in an effective manner in the service routine. Making this strategy possible requires training of the teams and an action committed with the continuity of the service and the efficiency of the results, in view of the priority in the TB control among the indigenous communities.

PS-100478-14   Development of action for tuberculosis diagnosis in the primary health care services, Pelotas, Brazil

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Aim: To describe actions developed at Primary Health Care (PHC) services for the diagnosis of tuberculosis

(TB) in Pelotas, Brazil, according to the patient's perception.

Methods: A descriptive study, quantitative approach, using data from primary source by applying a structured questionnaire to 102 TB patients in treatment at health care units with traditional Tuberculosis Control Program (TCP) in 2009. The data were analyzed using descriptive statistical techniques.

Results: Among patients, 34.3% ($n = 35$) first sought PHC services (Family Health Strategy Health Centers or traditional Health Care Centers) when realized feeling ill, and 68.6% of these patients got an medical appointment in the same day of health services' first visit. Only 28.6% of patients received a sputum smear test request, and 54.3% received an X-ray request. 54.3% were referred to other health services for medical consultation with another professional. Regarding to local where diagnosis was made, only 20% obtained the diagnosis confirmation in the same health service of first consultation, the majority (42.9%) was diagnosed at TCP units. The median time to obtain the diagnosis of patients who sought PHC services was 30 days, and 75% got the diagnosis until 60 days.

Conclusion and recommendations: The study shows a weakness of PHC performance for TB cases detection and diagnosis. This may be related to lacks in involvement of local authorities in TB issues, low coverage of the Family Health Strategy, quantitative deficiency of human resources and neglect of health professionals in symptoms investigation. It is considered that incorporation of search and detection of TB cases activities in the Brazilian context of health system decentralization requires a health professionals training policy in PHC services in order to improve their responsibility in TB control.

PS-100255-14   Health services organization, patient characteristics and time of diagnosis, Ribeirao Preto, Brazil

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Aim: To describe patients' characteristics and health services' organization for the diagnosis of TB in Ribeirão Preto, Brazil, in patient's view.

Methods: Epidemiological study, survey type. The study population consisted of 101 TB patients in treatment. Data were collected between July–December 2009 through a structured questionnaire and analyzed using descriptive statistical techniques.

Results: Patients were mostly male (69%), caucasian (46%), married (41%), Catholic (60%), none to eight

years of education (79%), unemployed (33%), with a mean age of 41.4 years (± 15.4). 84.2% were pulmonary TB. 70% of respondents search for health facilities when feeling sick. The median time between onset of symptoms and first visit for health services was 15 days, and 75% until 30 days. The median time for getting an appointment at first health service accessed was 0 days, 1 day for 75% of patients. The Emergencies services were the most accessed local (56%). Sputum examination was requested for only 46.5% of the suspects at the first health service sought; X-ray was requested for 74.3%. Most of TB suspects (64.4%) were referred to other health services for medical consultation. Reference centers with Tuberculosis Control Program (TCP) and emergency services accounted the majority of TB diagnoses (30.7% and 26.7%, respectively). The median time interval between the first consultation in a health service to diagnosis of TB was 7 days, and 75% until 30 days.

Conclusions: Emergencies services were first facility accessed, and the diagnosis was more attached at TCP, followed by emergencies services, which is consistent with centralized way that TB control is organized in Ribeirão Preto. Delay of patient in care seeking, difficulties in obtaining appointments and low sputum smear request were elements found on the process of obtaining diagnosis in the city.

PS-101111-14   Patient and health service delay in the diagnosis of tuberculosis in Foz do Iguaçu, Brazil

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Aim: To analyze characteristics of patients with tuberculosis (TB) and resolution capacity of first contact services for diagnosis.

Methods: A descriptive study, survey type, quantity approach. 101 TB patients were interviewed in Foz do Iguaçu—Brazil, in 2009. The data were analyzed using techniques of frequency distribution, average, standard deviation (SD) and median.

Results: Prevalence of male patients (65.3%), according to race/ethnicity, 45.5% were caucasian and 39.6% brown-skinned, married or living in stable relationships (53.5%), with zero to eight years education (66.3%), without paid professional activity (44.6%) and mean age of 37.2 years (SD = 13.8 years). The average TB patient' family income was 1146.00 BRL (SD = 1290.00 BRL), with an average income per capita of 297.60 BRL. However 54.5% of households received between zero to two minimum wages, and for them, the average income per family member

declined to U.S. $139.50. When feeling sick, for what-ever reason 72.5% of respondents reported looking for health care facilities. However, only 22.7% go frequently for a preventive health check up. The median and 75th percentile of time elapsed between first symptoms and first search for a health service was 21 and 60 days, respectively. Although most patients have sought emergencies services (36.6%) and Family Health Units (25.7%), most diagnoses (50.5%) were carried out at reference units with Tuberculosis Control Program. The median time elapsed between first search for a health service and diagnosis was 14.5 days, 75% of respondents had their diagnosis made within 30 days after health care seek.

Conclusion: There was a considerable delay in detection of TB cases due to factors related to the patient. However, the total time delay of diagnosis was increased by health services' characteristics. Organization of health services in Foz do Iguaçu, with a strong vocation in curative care, possibly contributed to the delay observed in this study.

PS-100825-14   Diagnostic process of TB suspect in Jogjakarta, Indonesia: from algorithm to reality

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Background: TB control in high burden countries heavily relies on algorithms to diagnose pulmonary TB cases. Optimal case detection then depends on effective implementation of these algorithms. We assessed how the National TB Program algorithm is applied in primary health centers in Jogjakarta, Indonesia.

Method: We documented the diagnostic processes of all adult TB suspects registered between October 2009 to March 2010 in all health centers in Jogjakarta municipality. Data on patients' gender, age and symptoms were collected as well as data regarding types, dates and sequence of examinations, examination results and final diagnosis. We compared actual practice with the diagnostic algorithm of the Indonesian National TB control program that breaks down in twelve standard diagnostic pathways.

Results: Of 284 TB suspects identified, 51% were female and 20% were younger than 30 years. 42% dropped out during the diagnostic process. 70% of this dropout occurred after a first series of negative sputum smears and no effort at patient tracing. Of the 58% suspects that did not drop out, 10% were

diagnosed as smear+ TB, 3% as smear- TB and 45% as non-TB. 49% of all these were eventually diagnosed following diagnostic processes not in line with the national standard. Of those who were diagnosed not in line with the standard pathways, 88% were diagnosed as non-TB, 63% of them were diagnosed after a first series of negative sputum smears when the patients' symptoms disappeared.

Conclusion: Far too many TB suspects drop out early in the diagnostic process. Half the pathways followed were not in line with the national algorithm for TB diagnosis, but not necessarily irrational from a medical perspective. There is a need to minimize dropouts and to review the appropriateness of the existing algorithm.

TB MONITORING AND EVALUATION

PS-100397-14   Pretreatment economic loss in TB patients in Kashmir valley

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Setting: Tuberculosis (TB) remains the number one killer infectious disease affecting adults in developing countries. In most low- and middle-income countries, more than 75% of the TB patients are in the economically active age group of 15 to 54 years and thus, loss of family income due to a case of TB is often severe.

Objectives: To study the direct or indirect cost incurred by TB patients before they start treatment under RNTCP in Kashmir.

Methodology: This was a cross sectional study of tuberculosis patients registered under Revised National Tuberculosis control Programme in district Srinagar and Kupwara, conducted over a period of three months from 1st July 2008 to 30th September 2008. TB cases were identified from the Tuberculosis Register which is maintained at Tuberculosis unit.

Results: The mean age was 34.26 years. Almost in 80% of TB cases the monthly household income was < Rs.5000. Mean loss of days of wages/school was 7 days and mean expenditure till TB was diagnosed was 5221 rupees. Expenditure till diagnosis of TB in Srinagar (urban district) was Rs.5913 as compared to Rs.4481 in Kupwara (rural district) ($P = 0.045$). Mean expenditure in females was Rs.7840 whereas in males it was 3202 ($P = 0.01$). Pretreatment expenditure was more in patients with low income as compared to high income patients.

Conclusion: TB enhances poverty even though both diagnostic and treatment facilities are free under RNTCP because the main targets of TB are socio-

economically poor people in their economically productive age who are further drowned into poverty because of pretreatment economic loss in terms of expenditure and loss of days of wages.

PS-100101-14   Literature analysis of tuberculosis research of Hubei, 1995–2008

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Objective: As the Hubei provincial tuberculosis control project supported by World BankLoan and British donation is coming to an end, it is necessary to evaluate it from all aspects. In order to indirectly assess the effectiveness of the research, the author collected papers on TB published from 1995 to 2008 from CDCs at all levels, analyzed the characteristics and then categorized them.

Methods: Based on the published date, all the papers were stored in two groups, the 1995–2001 group and the 2002–2007 group. Using bibliometric methods, the author, journal, date of publication, research institution and abstract information were extracted, and an excel database for statistical analysis was established.

Results: The number of literature exhibited a steady and gradual increase from 2 in 1995 to 50 in 2007. Only 3 papers in the 1995–2001 group were published in corelibrary journals, while 9 papers were published in the 2002–2008 group. The Hubei Provincial CDC, Wuhan CDC, and Yichang CDC contributed to the majority of the literature, accounting for 75.6% during 1995–2001 and 58.9% during 2002–2008.

Conclusions: The launch of the two projects led to vast improvement in research capacities in TB control. From 1995 to 2008, the number of the literature increased steadily and the quality improved. However, there was still some substantial difference between regions. In some regions, the research capacity was stronger, while in some regions was not strong enough. Therefore, the central TB project board should pay adequate attention to the latter areas so as to gradually narrow the gap.

PS-100105-14   The economic evaluation of Hubei WB/DFID TB control project

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Objective: To analyze the health-economic benefits of Hubei WB/DFID TB control project from 2002 to 2007 and provide scientific basis for sustainable development of TB control in the future.

Methodology: Data of Hubei WB/DFID TB control project was collected from Huber CDC. In addition, questionnaires were used to collect some other essential data. Three main health-economic techniques namely CEA, CUA, CBA were adopted. Economic benefits were analyzed from the direct, indirect and potential ways.

Results: From 2002 to 2007, 184 694 active TB patients were find, 173 195 were cured. A total of RMB125.4 million Yuan was invested in this project. The discover and cure cost of one patient on average was RMB 724 Yuan. DALY of 1 825 302 year was directly saved, 1 614 525 healthy people avoided contacting tubercle bacillus thus reducing 193 743 TB cases. A loss of GDP RMB 20.27545 billion Yuan was avoided, as well as a loss of Huber province personal disposable income RMB 17.88796 billion Yuan. The directly economic benefit of this project was RMB 623.42 million Yuan, the indirect, RMB 742.24 million Yuan, and the potential, RMB 1.61465 billion Yuan. The total economic cost/benefit ratio is 1:23.8.

Conclusion: In accord with the low-input, high-output economic principles, Hubei WB/DFID TB control project is a typical disease control example worthy to be learned and promoted with its high feasibility and significant economic benefits.

PS-100176-14   Health system strengthening through web-based TB care and monitoring systems in Uganda

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Background: According to WHO, the 3rd health system strengthening block is Information and knowledge systems. While enormous resources have been geared towards improving other five blocks especially medical products, little efforts have been allotted towards improving knowledge information systems to capture, store, analyse and report about epidemics promptly and consistently to for decision and policy making. In Africa, TB is a huge public health problem considered to be the leading killer of people living with HIV/AIDS. TB management can only be successful by promptly identifying and reporting TB cases in the communities, start treatment and followup to ensure adherence and treatment completion.

Methodology: With improvements in IT, such as internet, new information management systems that promptly provide access to vital data on incidences, prevalence and treatment levels are urgently needed keep accurate and updated records of TB patients and drugs for followup and reporting. A web based system designed using HTML, php and mysql relational database was developed to quicken data capture, reporting and notification of TB cases in the community. The system was tested in 14 Health Units using 14 data entrants, 7 supervisors and 3 Managers who noted it's effectiveness in data capture and criti-

cal alerts on missed drugs refills, relapses, defaulters and pending or upcoming drugs pickup.

Lessons learnt: 1) Implementation of this system has shown that a web-based system is ideal to not only eradicate delays in report submission, but also minimize error in data entry and loss in transit from collection points to districts and later to head office.

2) TB program managers are able to know the incidence, prevalence, success and failure rates of TB treatment in time to enable them make decisions on how much drugs, of what regimen and laboratory kits that should be procured to contain the epidemic.

PS-100229-14   Outcome assessment of a Global Fund Grant in tuberculosis control in rural Cameroon

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Setting: Batibo District Hospital, North West Cameroon.

Objective: To assess the outcome of implementing the Global Fund grant Round 3 in tuberculosis control at district level.

Design: A retrospective study for the period 2003–2008 comparing tuberculosis program outcome indicators before (2003–2005) and after (2006–2008) the Global Fund grant.

Results: A total of 293 tuberculosis cases were enrolled on treatment during the study period. Comparing the cumulative outcome indicators 3 years before and after the grant, case notification increased by >75%, case detection by almost 50% and treatment success by nearly 20% during the grant period. Analyzing annual variations, there was nearly a double increase in case detection rate (from 20% to 35%), while treatment success rate reached the ideal 100% in 2006 (from 72.8% in 2005). The defaulters and mortality rates were nullified in 2006 and 2007 from maximum values of 15% and 23% respectively in 2004 and 2005. However in 2008, there was a decline across all program indicators, probably due to staff turnover.

Conclusion: Outcome indicators of the tuberculosis program in Batibo District Hospital increased markedly with the Global Fund grant. Nevertheless, staff turn-over if not tackled appropriately might impede the sustainability of this positive outcome.

PS-100437-14   Developing user requirements for improving TB case referral and program supervision in Tanzania

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Background: Mobile technologies have great promise for improving processes such as the tracking of TB cases; however, the development of such systems is difficult because the gathering of user requirements in public health for low resource settings is not well established.

Intervention: We applied SARA, a Systematic Architected Rational Approach to derive user requirements for TB suspect identification and case management in Tanzania. This involved a Collaborative Requirements Development Methodology with stakeholders including: community health workers, sputum fixers, district and regional coordinators, and national officials.
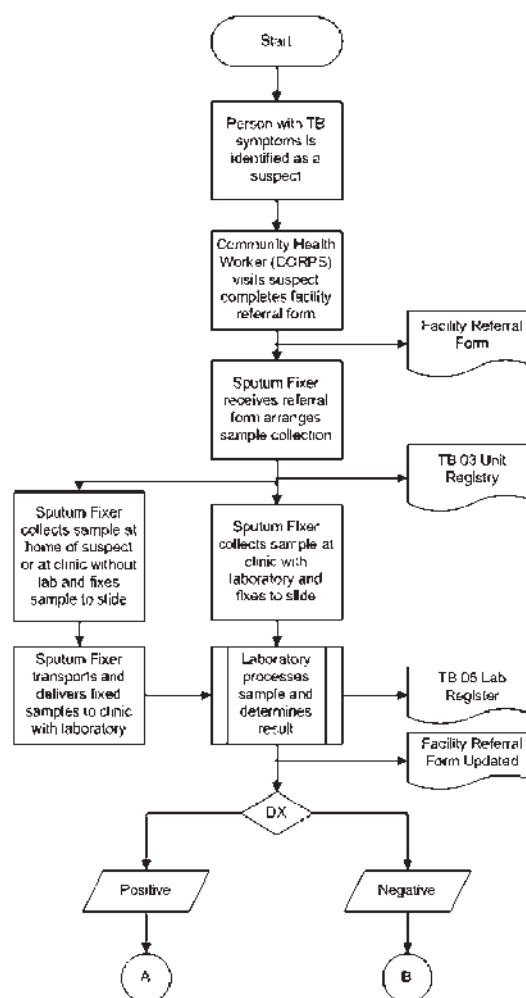

Figure   Tanzania TB Program Activity Diagram Case Identification to diagnosis version 1.0 last updated 2009-09-15.

Results: Participants identified referral at the community level as the most pressing problem since rural clinics often do not have facilities for sputum microscopy diagnosis of TB, so suspects are often referred great distances for testing. Other significant problems were the supervision of community based TB control staff and data reporting from the community level. TB program activity diagrams (a portion shown in the accompanying Figure) were developed in an iterative manner with the participants. These covered the TB case identification, diagnosis and treatment. This articulation of the work flow was the critical step in defining the process to allow the introduction of mobile technology and information system support. The existing paper forms provided important reference points for the work flow.

Conclusion: The collaborative methodology allowed stakeholders at different levels of the system to communicate, express priorities, and identify the key steps in the work flow. This made it possible for designers to capture the user requirements for systems supporting the management of TB. Based upon this information, we are currently implementing two mobile phone based systems, one to help community health workers track active cases of TB, and the other to support district TB managers in supervising facilities.

PS-100672-14 Modelo de evalucaión del programa de control de la tuberculosis

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En Brasil la evaluación es una acción aún poco utilizada para el planeamiento y análisis de los procesos y resultados. En la visión clásica, la implantación es una de las fases del 'ciclo de política', correspondiendo a la ejecución de actividades para alcanzar metas predefinidas. En otra perspectiva, la formulación e implantación de políticas representan un proceso sujeto a la influencia del contexto y de mecanismos intervinientes. La construcción de modelos teóricos permite que la evaluación de políticas y programas sobrepase la visión dicotómica insumos/resultados y posibilita la aclaración de las razones del éxito de la intervención en contextos diversos y para distintos grupos de poblados. Un modelo de autoevaluación fue propuesto para auxiliar el gestor en la identificación de problemas, en la caracterización de factores favorables a intervenciones exitosas y en la mensuración de los efectos. El gestor puede adaptarlo de acuerdo con preguntas evaluativas relevantes. En ese modelo fueron considerados los componentes sociocultural, político, organizacional, y asistencia, así como los recursos, actividades y los respectivos productos, y los efectos: resultados e impacto. Con base en los efectos esperados fue determinado el patrón de juzgamiento de la integralidad y calidad de las acciones, y utilizada la matriz de evaluación rápida para

aumentar el rendimiento. Los 3 estudios de evaluación de intervenciones para el control de la TB, que sirvieron como base para esta propuesta, se utilizaron de abordajes cuantitativas y cualitativas, distintos métodos de coleta de datos y múltiples fuentes de evidencia, aumentando la validez interna y reproductibilidad de modelo. Los principales resultados fueron la falta de autonomía técnico-gerencial; la carencia de recursos humanos, financieros y materiales; y la deficiencia en la integración entre programas para mejor rendimiento de las acciones de control.

PS-101272-14 A systematic review of economic evaluation studies of tuberculosis control in high-income countries

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Tuberculosis (TB) is a leading cause of death in developing countries and an important health threat in the developed world. Ideally, interventions in TB control are effective, acceptable, and economically attractive. This review summarizes all economic evaluation studies of TB control in high-income countries over the last 20 years. A total of 118 studies using different economic evaluation methodologies on a wide range of TB interventions were included. Most studies (70%) were from North America and about half (47%) studied interventions among the general population. Even though the large majority of studies (85%) aimed at preventing active TB disease, 44% of these ignored the prevention of secondary infections, thereby underestimating the benefits of the intervention. Choosing a healthcare instead of a societal perspective (92% vs. 8%) further underestimated the benefits. Moreover, 62% of the studies disregarded discounting and thus overestimated future costs. In all, 66% of the studies reported a favorable result, which is modest given that a publishing bias towards favorable results is to be expected. We conclude that many studies in this review have put the TB intervention studied at a disadvantage by the choice of methodology, i.e., underestimating benefits and overestimating costs. This may lead to an overly conservative approach to the introduction of new interventions in TB control.

PS-101307-14   Cost analysis of TB-HIV reduction models: enhance case finding and household interventions

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Background: This study was conducted as part of Zambia-South Africa TB and AIDS Reduction (ZAMSTAR) study. The four arms are the community-based enhanced case finding of tuberculosis (ECF), TB-HIV activities at household level (HH) and the control arm. Standardized TB-HIV activities were put in all arms (TB-HIV).
Objectives: To calculate the costs and cost-effectiveness of implementing ZAMSTAR interventions.
Methods: Economic costing of four arms of ZAMSTAR study was conducted from provider's perspective. The study was done in 16 communities in Zambia with a total population of about 850 000. Costs were collated from expenditure review and interviews. Costs were reported as full costs and average costs. Elasticity was used to compare the attractiveness of each investment with regard to TB-HIV. Elasticity is the measure of responsiveness. The intervention with large elasticity is less attractive.
Results: The average costs per additional smear positive TB case identified are US$81.82, US$398.92 and US$191.46 for ECF, HH and HH plus ECF strategies, respectively. The average costs per population were estimated at US$0.44, US$0.53 and US$1.12 for ECF, HH and HH plus ECF, respectively. See Table for details.

Table   Average costs and cost-effect responsiveness for TB case finding

Inter-vention	Cost/ additional TB screening (US$)	Cost/ sputum analyzed (US$)	Elasticity	Cost/TB case identified (US$)	Elasticity	Cost/ population (US$)
ECF	5.70	5.70	4.8	81.82	5.7	0.44
HH	5.45	118.14	37.1	398.92	30.0	0.53
HH plus ECF	11.44	13.77	5.8	191.46	13.9	1.12

* Positive.

Discussion: Cost-effectiveness analysis still underway. However, preliminary results from elasticity of outcome show that ECF is the most attractive. However, HH are additional benefits such as increase HIV activities such as VCT uptake, HIV testing and ART uptake and adherence. Thus TB outcomes are not a fair comparison for CE analysis. The better comparison would the use DALYs, QALYs or some other more universal benefit.

PS-101394-14   Continuous surveillance of anti-TB drug resistance: global capacity for representative data

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Introduction: Continuous surveillance of drug resistance is based on the routine collection of data on drug susceptibility testing (DST) of TB patients. It allows for appropriate and timely public health response. WHO guidelines advocate for the universal adoption of continuous surveillance in at least previously treated patients, and in all TB patients where technical and financial capacity allow. We classify the latest national TB surveillance data provided to WHO on criteria of completeness and quality.
Methods: Continuous surveillance data reported to WHO were classified as 'Class A' and 'Class B' based on 4 indicators. Data meeting all 4 of the following criteria are considered Class A, indicating a high degree of representativeness and accuracy: case detection rate >50%; positive culture in ≥50% of notified cases; DST results available in ≥75% of culture positive cases; accuracy of ≥95% for isoniazid and rifampicin in DST proficiency testing with a suprana-
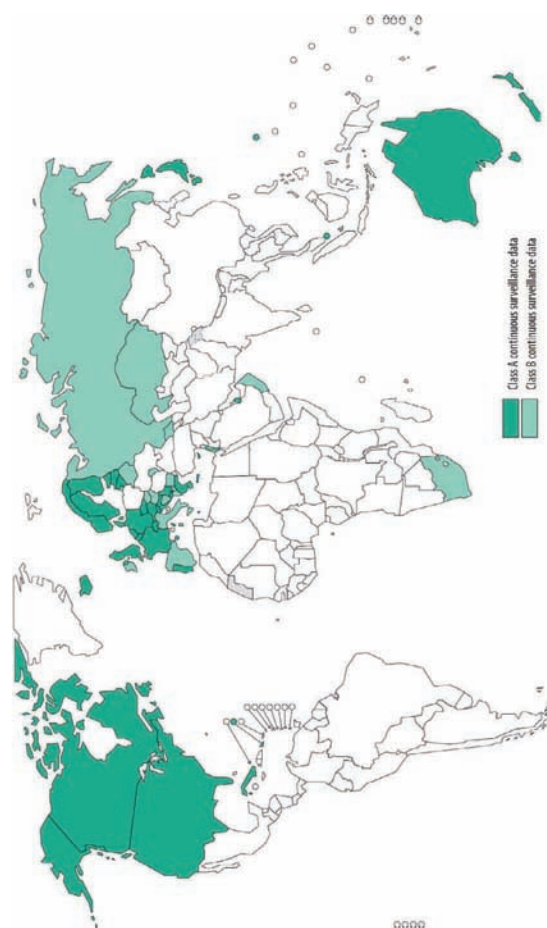

Figure   Countries with Class A and Class B continuous drug resistance surveillance data.

tional reference laboratory. Data not meeting Class A criteria, but meeting the following criteria are considered Class B, indicating a moderate degree of representativeness: Positive culture in ≥35% of notified cases; DST results available in ≥50% of culture positive cases.

Results: Countries providing Class A or B data for 2008 or 2007 are presented in the Figure. Less than one fourth of all countries (22%), provide data of Class A or B. While the majority of countries collecting Class A data are high-income, several middle-income countries are also able to provide such data. No low-income country, and no country in the African region (with the exception of South Africa) and the South-East Asia region, are able to provide Class A or B data.

Conclusion: The established classification criteria allow for the systematic evaluation and comparison of countries' surveillance systems, and as such can be used to advocate for the introduction of measures for attaining higher quality.

PS-101520-14   Monitoring and Evaluation network to control tuberculosis in Brazil

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The Monitoring and Evaluation (M&E) network proposal was launched in January of 2008. The 57 municipalities covered by the Brazilian Global Fund Project to control Tuberculosis adopted the network as a strategy. The networking group decided to establish four focal points. These points will be responsible for mobilizing the strength of Surveillance System and disseminate the M&E culture. The M&E Network has already joint the participation of governmental programs for tuberculosis, AIDS and Primary Care and several civil society members from local, state and federal levels. The M&E network has already been created. During these twenty-one months of existence, the M&E network proposed a collective assessment of epidemiological data analysis, discussions and actions undertaken by the government and the Global Fund Project. This process addressed the importance of planning actions using M&E data. The M&E network will provide a new way of information use through the practical application of it. The network will be an important influence to strengthen the use of the National Surveillance System among the policy makers and the civil society. The M&E network can evidence the real demand to control tuberculosis by data evidences and the sponsor's involvement.

TB-HIV EPIDEMIOLOGY

PS-100317-14   TB disease among patients receiving HIV care and treatment in a high TB prevalence setting

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Background: Tuberculosis (TB) is the leading cause of morbidity and mortality among HIV-infected persons; its impact can be reduced with antiretroviral therapy (ART) and TB treatment. Nyanza province in western Kenya has a 15% adult HIV prevalence and ~70% TB-HIV co-infection rate. HIV care services were introduced in 2003 and expanded rapidly. We describe TB disease among HIV patients receiving HIV care including ART, in the KEMRI/CDC Health and Demographic Surveillance System (HDSS) from 2003 to 2008.

Methods: Data were abstracted from adult patient medical charts in 20/57 (35%) health facilities providing HIV care in and within a 50 km radius of the HDSS. These 20 facilities provide HIV care to ~80% of HDSS residents. Abstracted data were linked with HDSS demographic and mortality data.

Results: A total of 4700 patient charts were abstracted and linked to HDSS data. Median age at enrollment was 34 years; 3125 (66%) were female and 2102 (45%) had baseline WHO Stage ≥ 3. At least 553 (12%) had prior TB history, 61 (1%) were diagnosed at enrollment and 192 (4%) developed active TB while receiving HIV care; 18 (3%) of who were a second TB episode. Patients with prior history of or active TB at enrollment had higher WHO staging at enrollment (≥3) compared to those who didn't (98% vs. 41%, $P < 0.001$). Patients were screened for TB at 14 (70%) of facilities. Cumulative mortality was greater among HIV-infected patients with a previous/current TB diagnosis or those who developed TB compared to those who never suffered TB (29% vs. 18%; $P < 0.001$).

Conclusions and recommendations: About 17% HIV patients had a prior history of TB, a current TB diagnosis or developed TB while on HIV care/treatment. These individuals had more advanced WHO staging at enrollment and greater overall mortality. Facilities had capacity to identify TB patients but there is a need to strengthen screening and develop/improve interventions to improve overall mortality among co-infected patients

PS-100599-14   Prevalence of HIV in tuberculous patients presenting to TB clinic of KDA Hospital, Kohat, Pakistan

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Background: Although HIV/AIDS is a rare disease in Pakistan, but severe and complicated tuberculosis occur in HIV positive patients. Screening for HIV in tuberculous patients was started in 2008 at Divisional Headquarters Hospital Kohat, which is in the North West Frontier Province of Pakistan.

Method: All tuberculous patients presenting at Tuberculosis Centre of Divisional Headquarters Hospital Kohat were screened for HIV with rapid test. A total of 939 tuberculous patients were screened since Jan 2008 till date. Out of these, nine patients had reactive rapid test which was confirmed on ELISA test. These patients have been registered at ARVs Centre Kohat and their CD 4 count was performed and treatment for tuberculosis was monitored.

Main findings: 9 out of 939 (0.95%) of the individuals were rapid test positive. The male to female ratio was 7:2. The response to Anti tuberculous treatment was good in these patients except in those with low CD 4 count.

Conclusion: We found an overall prevalence of 0.95% HIV in tuberculous patients. Males are predominantly affected as compared to females. Rapid test should be advised to all tuberculous patients.

PS-101013-14   HIV-infected patients with tuberculosis in St. Petersburg penitentiaries

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The goal of this research is to identify the specifics of TB course, in relation to drug-resistance of *Mycobacterium tuberculosis* in patients with HIV-infection kept in penitentiaries.

94 TB patients were investigated, in whom mycobacterium TB production has been confirmed by culture, as well as confirmed results of *M. tuberculosis* sensitivity to TB medications. All the subjects were divided into two groups. The main group (MG) was comprised of 46 TB-patients with HIV-infection. The comparison group (CG) was comprised of 48 TB-patients, HIV-negative.

Previously 30.4% of MG patients suffered from TB, and 43.8% of CG subjects suffered from the same. Local lung TB in HIV-positive patients with TB has been diagnosed 1.75 times less, than in HIV-negative patients. At the same time, 29.6% of the HIV-positive TB patients had disseminated processes, which is twice more than in HIV-negative patients. Isolated pleura TB could be diagnosed only in HIV-positive patients, while in the CG no such subjects were present. It has to be said that multiple TB focalizations could be seen in 34.4% of the MG subjects, which is approximately 3 times more than in the CG, where there have been only 11.1% of cases ($P < 0.05$). Among those who had already been suffering from TB, the infiltrating TB could be diagnosed in 50% of the patients in both groups. Lung tissue degradation could be seen in 59.4% of the MG patients (TB, HIV-positive) and in 77.8% of the CG patients, which is 1.5 times more. Additionally, for those with relapse of TB no difference has been revealed between the groups and degradation were diagnosed in 100% cases in MG patients and 95.2% patients in CG. Drug-resistance of TBM to TB medications to streptomycin has been revealed in 3.1% of the MG patients and 11.1% of the CG. Polyresistance, i.e. TBM resistance to two or more TB drugs has been seen in 31.3% HIV-positive and 37.0% of HIV-negative TB patients. In patients with relapse of TB polyresistance has been seen in 50.0% of the MG.

PS-101430-14   Prevalence of HIV infection among tuberculosis cases enrolled in DOTS settings in Egypt

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Methods: All TB patients detected in TB health facilities during the first quarter 2009 were enrolled in the study. TB diagnosis, treatment and HIV testing were done according to the national guidelines. Blood samples were collected for anonymous HIV testing. STATA software was used analyze to determine the prevalence of HIV infection in TB patients and in-depth interview through questionnaire to determine the risk factors for HIV infection and the pathway of health care.

Results: Of the 1923 TB patients enrolled, only 1465 accepted to undergo testing (76.2%) for HIV. Only 5 out of the tested patients (0.3%) were HIV positive. The rate of HIV infection was higher in TB patients from urban (Cairo & Giza) 60% (3/5) than rural areas 40% (2/5). The willingness to test for HIV infection in Upper Egypt 64.9% (432/666) was less than the other areas with no significance differences (great Cairo (78.2%), lower Egypt (85.5%), Costal governorates (83.7%), Frontier governorates (79.7%). 78% of the TB patients enrolled in the study were males (996/1465), 32% were females (469/1465). Age mean was 37 (SD 37.5 ± 15).

Conclusion: In general, the prevalence of HIV infection in TB patients was as low as 0.3% higher.

PS-100868-14   Improving access to HIV-TB services in the Soghd Region of Tajikistan

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Background and challenges to implementation: In 2009, there were 428 PLHIV and 1029 TB patients officially registered in Tajikistan's Soghd region. The mortality rate among patients with HIV-TB co-infection was 46% (death occurred in 5 out of 76 cumulative cases). Existing healthcare services cannot provide adequate access to HIV and TB diagnostics for PLHIV and TB patients.
Aim: To improve access to HIV-TB prevention, diagnostics, care and support for PLHIV and TB patients.
Intervention: Through its project, 'HIV/AIDS and HIV-TB Collaborative Activities in Central Asia', AFEW develops client management services in Tajikistan, Kazakhstan, Kyrgyzstan and Uzbekistan. In Soghd, AFEW has established 8 social bureaus (SBs), a service provider network and referral system that provide integrated HIV-TB services.
Results: The project has significantly improved the accessibility and quality of HIV and TB services in Soghd. Service provision to PLHIV has increased 3.27 times—up from 339 services in 2008 to 1111 in 2009. Altogether, 124 PLHIV underwent full testing for TB. The number of HIV counselling and testing services accessed by TB patients increased from 952 in 2008 to 1425 in 2009. Early TB diagnosis, treatment and care were also delivered to 18 patients with HIV-TB co-infection. 100% of patients expressed satisfaction with the quality of services.
Conclusion: A client management approach provides PLHIV and TB patients with better access to medical and social services. Active interaction between the NGO and state sectors leads to more effective prevention and earlier detection of HIV-TB co-infection.

PS-101279-14   Tuberculosis en Pelotas, Brasil: percepción de los enfermos que procuraron el servicio de salud, 2009

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Objetivo: Identificar la percepción de los enfermos que procuraron el servicio de salud sobre la tuberculosis en el município de Pelotas/Brasil.
Métodos: Estudio descriptivo de abordaje cuantitativo, realizado a partir de cuestionario estructurado, aplicado a 102 personas residentes en el municipio de Pelotas (RS), que procuraron el servicio de salud y realizaron el diagnóstico y tratamiento para tuberculosis en el año de 2009.
Resultados: De los 102 enfermos entrevistados 78,4% presentaron TB pulmonar, 19,6% extra pulmonar y 2% ambos, 12,7% presentaron VIH como enfermedad asociada y 14,8% aun esperaban resultados. En relación al conocimiento sobre la tuberculosis antes de estar enfermos, 52,9% lo clasificaron entre 'muy malo' o 'malo', 36,3% clasificaron la presencia de los síntomas como débiles a moderados y 63,7% como fuertes, 66,66% no buscaron el serviço de salud más próximo de su casa, demorando un tiempo mediano de 15 dias (escala 1–1095) para buscar el servicio de salud, siendo el más buscado el servicio de atención primária (54,9%), seguido por los servicios de complejidad secundaria (27,5%), emergencia (26,5%) y hospitales (10,8%).
Conclusión: El estudio revela carencia de conocimiento sobre la enfermedad en personas que presentaron predominantemente la forma clínica con mayor riesgo de contagio, llevándolos a buscar los diversos tipos de servicios de salud en los diferentes niveles de complejidad del sistema. Se considera la necesidad de acciones educativas con abordaje individual y colectiva sobre la tuberculosis, énfasis en la valorización de los síntomas y sensibilización de los profesionales de la salud que actuan principalmente en los servicios de atención primária, para potencializar la accesibilidad y utilización de servicios de salud más próximos de los enfermos.

PS-100335-14   Tuberculosis and HIV co-infection in Denmark, 2007–2008

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Background: Is examination for HIV infection increasing among tuberculosis (TB) patients in Denmark (DK)? What is the true rate of TB with HIV co-infection?
Method: It was investigated whether patients notified with TB in Denmark (DK) in 2007 and 2008 had been examined for HIV infection.
Material: TB was notified for 392 patients in 2007 and 367 patients in 2008.
Results: HIV infection was examined in 160/392 (41%) of TB patients in 2007 and in 178/367 (49%) in 2008. Number of HIV infected identified was 12 in each year. Examination for HIV depended mainly on age. Frequency of HIV examination was nearly the same in Danes and immigrants. HIV infection was found in 3% of all TB patients in 2007 and 2008, and in 8% and 7% of those examined in the two years, respectively.

Discussion: Many treatment centers include examination of HIV infection among TB patients in their instructions. It came as a surprise for many in 2008 that they did not follow their own instructions. The National Board of Health repeated the recommendation of examination of HIV infection in all TB patients by the end of 2009.

Examination for HIV infection was mainly performed in TB patients considered at risk, so the true level of TB with HIV co-infection cannot be calculated directly. It is likely that HIV infection rate was lower among TB patients, who were not examined, than it was among those examined.

Conclusion: Examination for HIV infection in TB patients increased from 2007 to 2008. This increase will probably continue with further attention to TB patients as a risk group of HIV infection also in DK and with strengthening of recommendations of examination for HIV infection in all TB patients. The true level of TB HIV co-infection in DK is likely to be 3–4%.

PS-100862-14   Changes in the HIV-infected tuberculosis patients in a city with a high level of coinfection

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Background: Many cities had three simultaneous epidemics during the 1990s: TB, HIV, and injecting drug use (IDU). The impact of HIV-infected IDU on TB was important and contributed to incidence increases.

Aim: To compare the characteristics of HIV-infected TB patients between 1990–1995 (pre-HAART period) and 1998–2008 (HAART implemented).

Setting: Barcelona, Spain.

Methods: Cross-sectional study on TB-HIV patients detected by TB Program residing in Barcelona. Sociodemographical factors, HIV transmission routes, prison history, use of directly observed therapy (DOT), treatment outcome and period of TB diagnosis (pre-HAART vs. HAART) were analysed by logistic regression using the odds ratio (OR) with 95% confidence intervals.

Results: From 1990–1995, 1523 patients were diagnosed and from 1998–2008, 715. The percentage of TB-HIV raised to 30% in 1994. In 1996, it declined to 7% by 2008.

Patients from the second period were older (median age 38 vs. 31 $P < 0.001$) more women were present OR = 1.4 (95%CI 1.1–1.8) and more foreigners OR = 3.4 (95%CI 2.4–5). There was less prison history OR = 0.12 (95%CI 0.1–0.2), but more homelessness OR = 2.6 (95%CI 1.6–4.4). Regarding route of HIV infection, we observed an increase in heterosexual transmission, OR = 1.6 (95%CI 1.1–2.4) and no changes in IDU. There was an increase of DOT OR =

24 (95%CI 16–36), less risk of death OR = 0.4 (95%CI 0.2–0.7) or lost to follow-up OR = 0.4 (95%CI 0.2–0.8).

Conclusion: Public health policies like free HAART and DOT, especially among the IDU population in methadone programs, have positively contributed to the TB-HIV epidemics. We must now maintain these policies and be aware on emerging vulnerable populations such as foreigners and homeless.

PS-100213-14   The analysis of effect with treatment and management of TB-HIV patients in Xinjiang

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Objective: Analysis the effects of TB-HIV patients with TB diagnosis, treatment and management in Xinjiang, and provide a reference for the development of TB-HIV patients with tuberculosis countermeasures.

Methods: With funding of the Global Fund 5 for TB control projects, TB patients has been conducted in HIV antibody test, That can be follow-up to the HIV/AIDS patients with TB checks, for the two-way screening found in the TB-HIV patients, management of patients receiving free anti-TB drugs, treatment, monitoring and management services for DOT.

Results: In 2007 the region had found 116 cases of TB-HIV patients and accepted by DOT for free anti-TB treatment management, Full supervision of the rate of 77.6%, Adverse reactions rate of 24.1%, Treatment success rate of 53.4%, Loss rate of 6.9%, Mortality rate 15.5%. TB patients in which 96 cases (82.8%), Full supervision of the rate of 82.3%, Adverse reactions rate of 21.9%, Treatment success rate of 58.3%, Loss rate 8.3%, Mortality rate 11.5%; 20 cases of extrapulmonary TB patients (17.2%), Full supervision of the rate of 55%, Adverse reactions rate of 35%, Treatment success rate of 30%, Mortality rate 35%.

Conclusion: Gradually increasing among TB patients HIV antibody testing and HIV/AIDS efforts in the discovery of TB patients, Vigorously promote TB-HIV patients with free treatment, supervision and management, Can improve the TB-HIV patients with treatment success rate and reduction spread of TB in HIV/AIDS patients.

PS-100349-14   Surveillance of TB-HIV co-infection in Europe

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Background: Tuberculosis (TB) and HIV/AIDS are global public health problems with considerable mutual interaction. In Europe our knowledge of the TB-HIV co-infection problem is limited. Surveillance is critical for measuring the burden of and controlling TB-HIV co-infection. We assess to what extent information on co-infection status is collected by national surveillance systems.

Methods: Questionnaires were distributed to all national EU/EEA TB and HIV contacts points of the European Centre for Disease Prevention and Control. Questions focussed on collection of data on TB-HIV co-infection status, burden of TB-HIV co-infection, data confidentiality, legislation, testing practices and perceived limitations and barriers to collecting TB-HIV co-infection data in the country.

Results: From 30 countries we received 25 TB and 22 HIV responses. Patients' HIV status was collected in 18/25 TB surveillance systems, with the majority of countries (16/18) relying on clinician reporting (two countries relied on data-linkage between the TB and HIV systems). Over half (14/22) of the HIV surveillance systems collected TB status; however 5 of these recorded TB status only if it was an AIDS-defining illness. The proportion of TB cases co-infected with HIV ranged from 0 to 15%, while the proportion screened for HIV ranged from 20 to 90%. Identified barriers to co-infection surveillance included poor collaboration between TB and HIV clinicians/surveillance departments, anonymous reporting and testing of HIV cases and lack of resources.

Conclusion: Information on the burden of TB-HIV co-infection is available in 21 EU/EEA countries, but methods of data collection and screening practices varied. It is recommended that efforts be made to collect this information in all EU/EEA countries including episodes of co-infection occurring after AIDS diagnosis, as well as indicators on screening of patients and demographic and clinical information to allow interpretation of these data.

PS-101409-14   Prevalence of non-tuberculous mycobacteria in HIV patients, Upper North Thailand

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Background: Non-tuberculous mycobacteria (NTM) is considered an opportunistic disease for those who are currently living with HIV/AIDS in Upper North Thailand. Because of high death rate (15–28%) in TB patients in each year.

Methods: We conducted a prospective study of patients with HIV infection and had TB suspected by symptom from 4 provinces 18 hospitals in Upper north of Thailand during 2006–2007 by collected sputum culture for *Mycobacterium tuberculosis* with indirect methods and Identify all strains with molecular technique (PCR REA).

Results: 474 of HIV positive had recruited and found that 139 case were positive culture for mycobacteria. All positive culture had identified as *Mycobacterium tuberculosis* complex (MTC) 66.9% and NTM 33.1%: 16 strains (11.5%) were *M. scrofulaceum*, 11 strains (7.9%) were *M. avium* complex, 5 strains (3.6%) were *M. kansasii*, 5 strains (3.6%) were *M. gordonae*, 3 strains (2.2%) were rapid grower, 4 strains (2.8%) were unclassified group III and 1 strain (0.7%) was *M. intracellulare*.

Conclusion: This study showed that TB-HIV in Upper North of Thailand were highly cause of NTM. If left untreated, NTM infection can cause abscesses bone, joint infections and infections of the lymph nodes, lung or soft tissue. Widespread infections can lead to serious illness and even death. So NTM and *M. tuberculosis* should be the majority of deaths in TB and HIV/AIDS patients in upper north of Thailand. Early access to ART with monthly testing and monitoring may help lower the risk of infection and may help prevent infections from spreading to untreatable levels.

TOBACCO SMOKE FREE INITIATIVES: FACTORS AFFECTING OUTBREAK INVESTIGATION/ PREVENTION PROGRAMMES

PS-100543-14   How effective is brief smoking cessation counselling in infertile couples?

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Introduction: Infertility is an important social concern. Environmental factor as smoking and tobacco consumption can affect sperm and follicular function and infertility. Smoke cessation reduces its complication and makes infertility treatment more effective which motivate and encourage infertile smokers to consider quitting.

Materials and methods: This is a descriptive cross-sectional study. Smokers referred to Avicenna infertility clinic with complain of primary infertility during 2008–2009 were studied. Required data were collected through questionnaire. They received tobacco cessation brief advice and educational material package of ill effects of tobacco consumption on general health and infertility. Success in quitting was assessed 6 months after the first visit.

Results: 70 cases were studied with mean age of 36.45 ± 6.3 which 68 (97.1%) were male. The mean of smoke consumption duration was 17.78 ± 7.49 & in fertility duration mean was 5.56 ± 4.0 year. Forty one individuals (59.4%) had mild nicotine dependence. Mean knowledge level about tobacco harms was 0.57 ± 0.79 (from total of 4 points) and attitude mean was 18.50 ± 2.95 (from total of 24 points). Estimating quit success rates, 41 individuals (63%) quit but it was unrelated to cessation factors.

Conclusion: It seems according to high motivation of this group, smoke cessation brief advice and increasing knowledge through educational package is effective. It is recommended smoke cessation brief advice and knowledge increasing be added to infertility treatment program.

PS-100739-14   Smoking cessation in chest diseases clinic and the role of pulmonary function test

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Aim: Smoking cessation is more easier for those who are effected by tobacco. Physicians' role is important in stopping smoking especially to those who apply to clinic. In this study, the effect of smoking cessation advice with the help of pulmonary function test (PFT) and patient's symptoms was evaluated.

Method: Symptoms, PFT findings and diseases were explained to the patient and he/she was adviced to stop smoking and admit one week later. In the second visit, improvement in symptoms and PFT findings were discussed with the patient and they were adviced to live without smoking. Patients with two PFT results were included to the study and the change in PFT findings were analysed.

Results: Thirteen of the total 48 patients were females. Mean age was 47.4 ± 12.1, smoking duration was 26.4 ± 12.8 years, daily cigarette consumption was 16.5 ± 10.2. Two PFT findings with a median interval of 10 (4–87) days were as follows: FVC $77.8\% \pm 18.8$, and $84.6\% \pm 19.8$; FEV_1 $67.1\% \pm 22.3$ and $73.6\% \pm 23.4$; FEV_1/FVC ratio: $69.9\% \pm 12.2$ and $70.7\% \pm 12.9$; FEF25–75: $46.1\% \pm 28.1$ and $70.7\% \pm 12.9$, respectively. Increase in parameters after stopping smoking were statistically significant other than FEV_1/FVC ratio. Rate of those whose PFT parameters increased after stopping smoking were 73% in FVC, 79% in FEV_1 and 67% in FEF25–75. In the first visit, cough and dyspnea were 72% and sputum was 43% present; in the second visit, symptoms did not change in 11%, increased in 64% and significantly increased in 24%. Two cases did not stop smoking, only decreased the amount in this short period, all others stopped.

Conclusion: With these findings, it is shown that symptoms and PFT findings can be used effectively in the clinic for stopping smoking. Smoking causes mostly small airway obstruction (decrease in FEF25–75); short term stopping smoking resulted in increases of FVC, FEV_1 and mostly FEF25–75.

PS-101028-14   Gender-related consideration on smoking cessation

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Setting: In the last years, different studies have shown the increasing of smoking habit among the women and argued that smoking cessation is more difficult among women comparing to men.

Aim: To analyse smoking cessation treatment, results and the withdrawal syndrome among women as against men.

Material and method: Retrospective study on 380 smoking women (age 39.5 11.3, Fagerstrom test 6.63 1.8) and 498 smoking men (age 38.5 10.8, Fagerstrom test 6.57 2.1) enrolled in STOP SMOKING

Programme in Smoking Cessation Center Craiova in the last two years. Data concerning age, dependence degree, smoking cessation treatment, results and symptoms of withdrawal syndromes were extracted from the patient files and were compared between the two gendres using χ^2 test.

Results: 32.36% of women and 35.74% of men wanted to quit smoking because of illness apprehension and only 15.26%, respectively 12.04% of men because of pre-existant disease; 52.10% of women and 51.4% of men invoked finances as a reason of smoking cessation. Varenicline treatment was recommended in 34.3% women and 39% men, while Bupropion treatment in 63.2% women, respectively 58.1% men. At 12 weeks of treatment, 61.1% of women and 65.2% of men were persistent quitters. Withdrawal syndrome occured at 52.4% of women and 54.7% of men. Main symptomes of withdrawal syndrome were hunger, somnolence, irritability, constipation and sweats.

Conclusion: Considering the treatment results and the occurence of withdrawal syndrom in smoking cessation, this study indicates significant statistical difference between the two genders, with a lower rates of cessation ($P = 0.0001$) and withdrawal syndrome ($P = 0.0009$) at women.

PS-100606-14   Advances in the control of tuberculosis in a suburban district of Paris, France, 2008

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Aims: The 'Hauts-de-Seine' district covers the suburban area located on the West side of Paris. It includes 36 cities and 1 532 000 inhabitants. The main duties of CLAT are to conduct TB case-contact investigations and to assure treatment and follow-up of TB cases and individuals with latent tuberculosis infection (LTBI). In 2007, 307 TB cases were identified and their 2539 family and professional contacts were investigated. Among the 145 cases of LTBI that were found, only 66% received RMP+INH combination for 3 months. In 2008, the goal was to treat all LTBI cases.

Methods: For each notified case of TB, (i) a CLAT physician makes contact with the notifying physician to collect basic information including patient address, type of TB, lab data, family and professional contacts, etc. (ii) Direct contact with the TB case is made by the CLAT nurse who fills in a complete questionnaire; (iii) Case-contacts are evaluated for both LTBI and active TB, and receive a tuberculin skin test and chest imaging, either in the CLAT or at a professional site. The evaluation is repeated 3 months later.

Results: In 2008, 269 TB index cases were notified, including 242 (15.7 per 100 000) living in the district and 143 living outside but having contacts in the district. The total number of identified contacts was 3027. The case-contact investigation found 9 (0.3%) TB cases and 126 (4.16%) LTBI cases, 101 adults and 25 children less than 15 years of age. All TB cases were successfully treated with the standard daily WHO regimen for 6 months. All LTBI cases were prescribed the RMP+INH combination for 3 months and up to now none of them developed TB disease.

Conclusion: We reached our goal of treating all LTBI cases but still do not know patient adherence to the preventive treatment.

PS-101298-14   Civil society participation in tobacco control in Bangladesh

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Background: Bangladesh ratified FCTC in 2004 and passed the National Tobacco Control (TC) Law in 2005. Since then the Ministry of Health and Family Welfare and NGOs are working together to implement the law. One of the important elements of TC law development and implementation is strong government and NGO collaboration at national and sub-national levels. Thus the capacity building of NGOs is crucial to strengthen the collaboration and implementation of TC law.

Intervention: To strengthen the smoke-free law implementation, four capacity building workshops on 'Tobacco Control Law and Smoke Free Policy Implementation' were organized in four divisions with the support of Bloomberg Philanthropies. Participants from NGOs, professional associations, media and academic institutes attended in the workshops. Effectiveness of each workshop was evaluated and priority actions were drown.

Results: A total of 109 participants attended in the workshops. Of them, 82.6% participants evaluated the overall workshop was very good; 82.6% accepted workshop was useful at work; 92.7% agreed group discussion and question/answer sessions were very good; 94.5% found handouts and materials were useful; and 89.0% participants mentioned balance between presentation and discussion was very good. Civil society members committed to keep their workplace smoke-free and support enforcement of TC law.

Conclusion: Increasing knowledge and building capacity of civil society for effective enforcement at district level are prerequisite for good tobacco control.

PS-100383-14 Super Army: unique school-based prevention programmes for poor city schools

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Objectives: High tobacco use rates in Indian children prompting a unique program called Super Army, especially for vulnerable children, creating sustained awareness through life skills and advocacy. The program has reached 77 238 slum children (12–16 year) through 147 government schools in Mumbai.

Methodology: Super Army, a two year interactive program that focuses on the holistic development of the child, through life skills, confidence-building and tackling peer pressure that are central to tobacco addiction. Messages are specifically designed using innovative media ideas that are child-friendly. The first year, uses theatre, art and creativity to build awareness and introduce life skills, team work, leadership, informed decision making to enhance self-esteem. Peer to peer learning is key. The second year focuses on creating advocates working on tobacco legislations and partnerships with stakeholders. Children work with civic authorities through tobacco control workshops that they conduct for the adult stakeholders. Sports and Arts training academies are designed for life skills development of potential peer leaders who are tobacco free.

Impact: Schools have extended intensive program from 2 years to 4 years because of decrease in tobacco use rate, heightened awareness and active advocacy (especially on tobacco law violation) in slum school children. Children continue as active tobacco control advocates even after graduating from the program, showing sustained commitment to tobacco control. Government has recognized impact and has given access to train schools across Maharashtra extending reach to 17 districts; 24 health workers; 10 937 teachers, 10 374 schools and 2 299 658 children.

PS-101467-14 Factors affecting chewable tobacco among rural women—a study in Jagatsinghpur district of Orissa, I

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Background: In January 2010 VHAI, an Indian health organization initiated an anti-tobacco campaign in Jagatsinghpur district under the framework of which a study was conducted to observe the factors affecting tobacco consumption habits of women in rural areas of Jagatsinghpur district.

Objectives:
—To assess the existing level of knowledge and practices on impact of tobacco use.
—To identify reasons of tobacco use among women.

Method: The study was conducted in 2 blocks of Jagatsinghpur district. There were 525 personal structured interviews and 6 numbers of FGDs organized to collect the quantitative and qualitative data respectively. Simple Random Sampling was used for sampling.

Results: Poor economic condition and lack of health education leads to multiple health risk in the community. Women in the community are over burdened with both house hold as well as out door activities. They get very little time in the day to look after their oral hygiene. They use ashes, mud or stick from the trees to brush their teeth. They use pond or river water for brushing and cleaning their mouth which they also use for bathing, cleaning utensils, cleaning after defecation etc. As a result of such poor oral hygiene practices, oral health problems such as infection, ulcer, cavity, bad breath, etc. are found. They try to hide these problems during the social interaction and intimacy with spouse. To avoid these problems most of the women consume tobacco products which becomes a habit and an addiction in long run. Tobacco habits also spread due to peer pressure. Social customs and rituals are also responsible for increasing use of tobacco among women.

Conclusion: This information can be shared with the Department of Women and Child Development, Health and Rural Development in order to deter tobacco use pattern.

PS-100143-14 Community-based 'Smoke Free Homes' interventions can reduce children's exposure to environmental tobacco

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Background: Children exposed to environmental tobacco smoke (ETS) have an increased risk of developing adverse health outcomes and becoming smokers themselves. The aim of this study is to evaluate the feasibility, acceptability and outcome of Smoke Free Homes (SFH), a community-based intervention.

Methods: SFH, designed to encourage families to implement smoking restrictions in their homes, was delivered over a period of six months through schools, healthcare settings and community events in Beeston, South Leeds, UK. It was evaluated using quantitative and qualitative methods including baseline and post-implementation surveys, focus group discussions and promise forms follow-up. The primary outcome measure was the difference in the proportion of households applying total smoking bans before and after implementation.

Results: We surveyed a sample of 318 before and 217 households after the intervention. The proportion of all surveyed households reporting being completely smoke-free significantly increased from 35%

(95%CI 30–40) at baseline to 68% (95%CI 61–74) 6-months post SFH implementation ($P < 0.0001$). Ninety per cent ($n = 62$) of people who were followed up by telephone 3 months after signing SFH promise form, said they were still keeping their promise at the time. Focus group discussions with participating children and parents conveyed acceptability of the intervention, in particular, the schools element, where children are encouraged to discuss the concept of SFH with the adults living in their households.

Conclusions: Our study shows that SFH can be implemented effectively and has the potential to improve children's health through preventing their exposure to ETS in the home.

PS-101411-14   Smoke-free initiative at sub-national level: a case study of Bogor City, Indonesia

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Introduction: Indonesia has the third largest number of smokers in the world. The current prevalence of smoking in Indonesia remains high, 65% in males and 5% in females. Smoking kills 200 000 annually and more than 97 million Indonesian non-smokers are regularly exposed to secondhand smoke (SHS).

Objective: To explore a successful smoke-free initiative of Bogor City.

Methods: Commitment of the local government is in place. Smoke-free local team was formed. City Health Office was assigned to lead the initiative. Smoke-free alliance was built of more than 40 NGOs. A legal and technical team in drafting and supporting local legislation and regulation was formed. Local evidences were collected such public opinion and air monitoring. Identified the champions in the local parliament and built their linkage with national tobacco control network such as Ministry of Health and NGOs. Series of policy advocacy and media activities were made.

Results: Bogor city has demonstrated that political commitment is the key for tobacco control. 100% smoke free policy was adopted. The policy ensures 100% indoor smoke-free in all public places and work places including public transportation. The policy also includes ban tobacco advertisement, promotion and sponsorship in the smoke-free areas. It also bans display of cigarette. The policy enters into force on 31st May 2010.

Conclusions: Bogor city provides a successful example of smoke-free at sub-national level in Indonesia.

PHENOTYPIC DETECTION OF TUBERCULOSIS AND DRUG RESISTANCE

PS-100268-14   Resistance pattern of *Mycobacterium tuberculosis* isolates from co-infected patients in Kinshasa, Democratic Republic of Congo

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Introduction: Kinshasa, the capital city of DR Congo, has 106 TB Clinics, centers for tuberculosis diagnosis and treatment. The activities of TB-HIV co-infection integrated in 5 TB Clinics: Bomoi, Lisanga, Boyambi, St. Alphonse and Mobengi. The co-infection TB-HIV activities implemented are VCT, HIV testing, and Co-trim and ARVs supply and social support.

Objective: To determine *Mycobacterium tuberculosis* resistance pattern and the impact of HIV infection on this resistance profile.

Methods: During 2 years 2008 and 2009, sputum collected from coinfected patients were sent to NRL in Kinshasa. Culture and first line drug susceptibility testing (DST) were performed on solid medium. The resistance pattern of *M. tuberculosis* strains was determined.

Results: A total of 409 cultures were recovered. Of the 77 *M. tuberculosis* strains isolated: 58 (75%) strains of *M. tuberculosis* are pansusceptible to the 4 first-line drugs; 9 (11.6%) resistant strains were retrieved. The profile of resistance is: 2 (2.5%) mono-resistant to Streptomycin, 1 (1.2%) polyresistant to Isoniazid, Ethambutol and Streptomycin and 2 (2.5%) resistant to both Isoniazid and Ethambutol. The rate of MDR-TB was 2.5%.

Conclusion: Most strains of *M. tuberculosis* isolated remain sensitive to first line drugs in Kinshasa despite the presence of HIV infection in TB patients.

PS-100274-14   Monitoring mycobacterial microcolony growth and rapid susceptibility testing on porous supports

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Background: The culture of mycobacteria for diagnostic and other applications remains of critical importance. Methods that can be practically applied in high burden labs are needed to reduce the delay in time to detection of culture and DST results. Notably microscopic observed drug susceptibility testing (MODS) has shown the potential to both speed up and increase the provision of mycobacterial culture in high burden settings.

Design: Here we explore the growth of *Mycobacterium tuberculosis* microcolonies on solid porous aluminium oxide supports, imaged by automated digital microscopy. This system allows the growth of microcolonies to be monitored individually, and critically, to change the media during the growth phase without disrupting the microcolonies. The ability to transfer colonies at any time onto selective media allowed us, within a few bacterial generations, to directly detect the drug susceptibility of individual microcolonies, and eliminates the need to either inoculate all samples directly onto selective and non selective media or re-culture positives on selective media and wait for new colonies to form.

Results: Colonies derived from laboratory cultures of TB could be detected within 4–7 days, and within 1–2 additional days the susceptibility for RMP could be detected. As the growth of individual colonies is monitored, the susceptibility of each colony could be detected, even when mixed susceptible/resistant strains were inoculated.
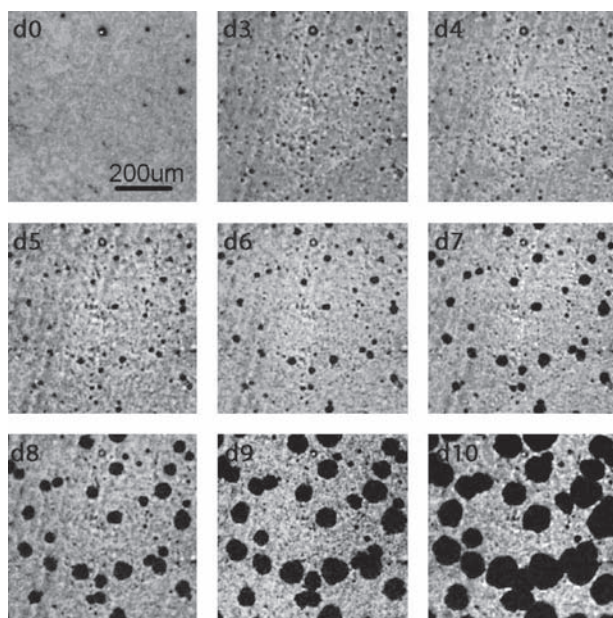
Figure Daily monitoring TB microcolony growth on porous supports between days 3–10. An automated microscope with 5× magnification was used.

Conclusions: Monitoring the phenotype of individual microcolonies as they grow has considerable potential for research, screening, and *M. tuberculosis* diagnostic applications. The method described is particularly appealing with respect to automation and safety as small numbers of cells are detected in a controlled environment.

PS-100755-14   Evaluation of thin layer agar culture and DST for sputum decontaminated with NALC-NaOH and CPC

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TLA is an inexpensive and sensitive method to perform culture and DST with a shorter turn-around time (TAT) compared to gold standard media MGIT and Löwenstein-Jensen (LJ). Cetylprydinium chloride (CPC) is an ammonium compound added to samples to partially digest and decontaminate samples during transport, but information on the compatibility of TLA for culture and direct DST method with this reagent is largely lacking. We evaluated culture performance of TLA versus MGIT and LJ for samples with or without CPC and TLA as direct DST method versus indirect MGIT-SIRE. We inoculated TLA plates with sediment from 77 smear-positive routine samples decontaminated with Nalc-NaOH: 44 without CPC and 33 with CPC. Samples without CPC were also inoculated on MGIT and those with CPC on LJ. For samples without CPC the positivity rate for TLA compared to MGIT was 93.9%, with an equal contamination rate (5.7%) and TAT of 9.3 days and 15.1 days respectively. For samples containing CPC, positivity rate for TLA compared to LJ was 83.3%. No contamination was observed on both media. The TAT was 12.9 days for TLA and 24.3 for LJ. Out of 40 DST available for comparison, TLA showed a sensitivity and specificity of 100% to correctly identify isoniazide and rifampicin resistance. CPC decreases contamination but also may retard and inhibit growth of mycobacteria. However, the increase of TAT may also partially be due to the presence of CPC-related debris on TLA which interferes with reading of the plates and thus delaying detection of microcolonies on the medium. TLA is a rapid method for culture of *M. tuberculosis* that may be applied also to samples containing CPC, providing results much faster than on LJ medium. To improve TLA performance with samples treated with CPC, use of neutralizing buffer to inactivate ammonium compounds should be further investigated.

PS-101043-14   Evaluation of Middlebrook 7H9 and MGIT for diagnosis of smear-negative pulmonary tuberculosis

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Objective: To compare the diagnostic yield of culture media Middlebrook 7 H9 and Mycobacterial Growth Indicator Tube (MGIT) against a conventional solid media culture for diagnosis of smear negative pulmonary tuberculosis.

Methods: Sputum specimens from patients coming from two hospitals in Lima with clinical suspicion of pulmonary tuberculosis and at least two negative smears were cultured in Middlebrook 7H9, MGIT and a classic solid media (Ogawa). A tuberculosis case was defined as one showing positivity for *M. tuberculosis* in any of the culture media.

Results: 520 non-contaminated samples were obtained from September 2005 to May 2008, out of which 148 (28.5%)were positive for *M. tuberculosis*. MGIT gave the best diagnostic yield with a sensitivity of 85.65% which was significantly higher than the obtained with Middlebrook 7H9 (77.87%) and Ogawa (65.98%). Middlebrook 7H9 also had a significantly better diagnostic yield than Ogawa. Growing times ranged from 3 to 72 days and were significantly shorter for both liquid culture media than for Ogawa ($P < 0.01$) but comparable between them (median growing time of 20, 20 and 29 days for MGIT, Middlebrook 7H9 and Ogawa respectively).

| | Ogawa | | | |
| | Positive | | Negative | |
	MGIT positive	MGIT negative	MGIT positive	MGIT negative
Middlebrook 7H9				
Positive	71	2	9	32
Negative	10	10	14	372

Conclusions: The use of liquid culture media for diagnosis of smear negative pulmonary tuberculosis can increase the sensitivity of culture in 20% compared with solid media alone, significantly shortening the growing time. MGIT gave the best results in terms of seinsitivity, but the growing time was comparable to Middlebrook 7H9. The concept of solid culture as the reference standard for tuberculosis should be revaluated at least for smear negative cases.

PS-101125-14   Detection of mycobacteria growth by direct microscopic observation of liquid cultures

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Bacteriological investigation is still the main tool in the diagnosis of tuberculosis. The results on solid culture media are generally obtained after three to four weeks while liquid culture permit a gain of about 7 to 10 days. More rapid results are obtained by molecular biology techniques but these are expensive and used only for smear positive cases. We implemented a new method of culture positivity detection based on direct microscopic examination of mycobacterial growth as described by Caviedes et al. We cultivated 63 samples (42 sputum and bronchial washings samples, 7 pleural fluids, 8 gastric aspirates and 6 pleural biopsies) in parallel on Löwenstein-Jensen media, MB/BacT and the new liquid culture method. Fourteen of these samples were smear positive (auramine- rhodamine stain). A total of 19 samples were positive on Löwenstein-Jensen, 17 on MB/BacT and 22 with the new method. Mean time to positivity ($\pm$ standard deviation) was 23.3 $\pm$ 4 days on solid media, 15.7 ($\pm$5.3) day on MB/BacT and 6.2 ($\pm$4) days with the new method. Three cultures were contaminated on solid media, four on MB/BacT and none with the new method. Direct microscopic observation of culture positivity is faster and more sensitive than both solid media and MB/BacT. The mean ($\pm$SD) time gain was 18 $\pm$ 6.4 days compared with solid media, and 11.6 $\pm$ 6.2 days compared to MB/BacT. The technique is easy and affordable.

PS-100173-14   Clinical variants of generalized TB among TB+HIV patients

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Aim: The main reason of TB+HIV patients' death in Saint-Petersburg is the development of generalized TB which clinical variants were investigated.

Methods: Complex study of 72 patients with co-infected pathology treated in TB hospital#2 during 2008–2009 was carried out and clinical data, CD4 and virus load (HIV-RHA), MBT detection and X-ray picture were appreciated. 64.2% of them were under antiretroviral therapy.

Results: It was shown that generalized TB was developed by three directions. Most favorable variant was co called generalized TB of lymphatic system with intrathoracic, peripheral, peritoneal, mesenterial and other lymphatic nodes affecting. This variant was characterized by frequent MBT excreting (62.4%).

CD4 level was on an average 381 ± 102 cell/μl and HIV-RNA was varied from 667 to 1 million/μl and more. Second variant was classic hematogenous generalized TB with development of military or large-focus lung dissemination, TB meningitis and TB dissemination of liver, kidneys, intestine and spleen. The majority of cases were without MBT excretion, CD4 were 100 cell/μl and less and HIV-RNA were more than 100 000 copies/μl. Third variant of generalized TB was found clinically more complicated. Cases were started as isolated damage lung or intrathoracic nodes with period of comparative clinical success when in first 1.5–3 month of treatment positive clinical, microbiological and X-ray dynamics was registered. After this period subsequent aggravation of patients' conditions with meningitis development and patients' death was fixed. This group of patients also didn't excrete MBT. TB progress was probably depended by immunity upsetting or metabolic damages which should been studied in future.

Conclusion: TB generalized cases were not equal by clinical and pathogenetic development but always proceeds on background of significant reducing of immunity and virus load.

PS-100070-14   The use of neural network for the diagnosis of pleural tuberculosis: can we avoid pleural biopsy?

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The diagnosis of pleural tuberculosis (PTB) is difficult because conventional tests of pleural liquid have low sensitivity and pleural biopsy for histopathological examination (HP) is an invasive procedure. New tests (ADA, ELISA and PCR in pleural liquid) are currently under study. Our objectives were to provide a computational tool to assist in decision making, identify risk factors and analyze the relevance of variables for the diagnosis of PTB. We used a database containing 135 patients with suspected PTB admitted to a general hospital in Rio de Janeiro, of whom 96 (71%) had PTB. Information included clinical variables (age, sex, smoking, HIV), diagnostic test results (conventional and new) and final diagnosis. Among traditional tests, HP had the highest sensitivity (77%). We used the Fisher Linear Discriminant (FLD) to maximize discrimination between the two classes (TB versus other diseases). We used two scenarios: pre- and post-test. In the pre-test one, information was extracted only from clinical data. In the post-test one, we added all the available variables (except histopathological examination and tissue culture, which involve biopsy). To refine the performance of diagnostic tests, we used artificial neural networks
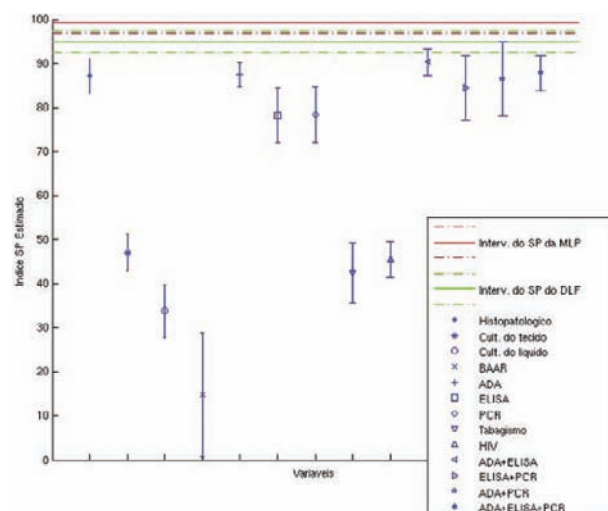
(Multilayer Perceptron, MLP). To match the conditions of the diagnostic results obtained by FLD and MLP, we divided the dataset into training and testing repeatedly, taking the average and standard deviation. In the pre-test analysis, both MLP and FLD achieved better performance than traditional tests. MLP performed better than FLD, ELISA and PCR. The performance intervals of HP, ADA, parallel combinations of new tests and MLP overlapped significantly, indicating that even without information on test results, the network was able to discern TB from non-TB as precisely as the best available tests. These results suggest the possibility of using neural network to avoid biopsy. Sponsored by FAPERJ, PIBIC/UGF, ICOHRTA and CNPq.

PS-100368-14   Diagnosis of pulmonary TB by MODS culture in HIV-positive patients

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Aim: Microscopic observation drug susceptibility assay (MODS) is a novel and promising test for the early diagnosis of tuberculosis (TB). We evaluated the MODS assay for the early diagnosis of TB in HIV positive patients presenting to Pham Ngoc Thach Hospital for Tuberculosis and Lung Diseases in southern Vietnam.

Method: All HIV-positive individuals suspected of tuberculosis, who were newly presenting to the HIV-TB ward at Pham Ngoc Thach Hospital from May to November 2008 were enrolled into the study unless they had received >8 days TB therapy. Data on socioeconomic and demographic features, TB history, TB contact history, HIV status and presenting clinical features were prospectively collected on a standard

case report form (CRF). Samples were collected for smear, MGIT culture and MODS culture.

Results: 738 consecutive sputum samples collected from 307 HIV-positive individuals suspected of TB were tested by smear, MODS and MGIT. The sensitivity of smear, MODS and MGIT were 56.9%, 70.7% and 74.9%, respectively against clinical gold standard (MODS vs. smear: $P < 0.001$, MODS vs. MGIT: $P = 0.03$). For diagnosis of smear negative patients, the sensitivity of MODS and MGIT were 37.7% and 45.1%, respectively ($P = 0.08$). The median time to detection of MODS and MGIT were 8 days and 11 days, respectively, and 11 and 17 days, respectively, for smear negative samples. Original bacterial/fungal contamination rate of MODS was 1.08% while it was 2.57% for MGIT. The cross-contamination rate of MODS was 4.74%.

Conclusion: MODS is a sensitive, specific and rapid test which is appropriate for detection of HIV-associated TB in developing countries.

PS-100417-14   Efficiency of combined use of solid media and liquid culture media in diagnosis of tuberculosis

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Background: Mycobacteriology Laboratories are integral components in the diagnosis and management of tuberculosis. This is not always possible as many settings are poor and faced with limited resources. As part of its Refugee and immigrant's relocation program, International organization for migration Laboratory Nairobi Kenya employed the use of both liquid and solid culture to increase its recovery rates.

Method: All samples were processed using the standard N-acetyl-cysteine (NALC-NaOH) method. 0.5 ml of already decontaminated sample was inoculated into an already treated MGIT BBL tube and 2–3 drops on Löwenstein-Jensen slants. A total of 1650 sputum samples were processed. Identification, were both tentative and confirmatory. For the tentative identification, it was based on colonial morphology, time to detection, visual appearance, and staining to check morphology. For the confirmatory it was done using capillia, Niacin and Nitrate tests.

Results: Out of 1650 sputum samples, 142 were *M. tuberculosis* whereby 28 were isolated on MGIT, 18 on LJ and 96 on both MGIT and LJ. The contamination rates were 9.6% and 6.3% for MGIT and Löwenstein-Jensen respectively. The mean time to detection was 14 days for MGIT and 28 days for Löwenstein-Jensen.

Conclusion: The use of liquid media is justified by increased sensitivity and reduced time to detection as opposed to Löwenstein-Jensen which takes longer time and low sensitivity. From positive specimens, preliminary identification on staining morphology

for presence or absence of cording as opposed to Löwenstein-Jensen can be done. MGIT is highly prone to contamination which is well catered for by low contamination rates of LJ, its colonial morphology is a mode of preliminary identification. Both systems complements each other in recovery, as what is missed by one system is captured by the other.

PS-100573-14   Field TB and MDR-TB diagnosis: the effect of delayed sputum testing

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Background: The complexity and biohazard of conventional sputum decontamination largely restrict TB culture with drug-susceptibility testing to reference laboratories. Thus sensitive TB diagnostics are often unavailable where they are most needed. Transport of sputum samples in disinfectant allows field testing for TB and MDR-TB. We studied the effect of delayed testing on results of sputum microscopy and field culture for TB.

Methods: Paired sputum samples were collected from 204 patients with suspected TB, half into a dry sputum pot for testing by Ziehl-Neelsen (ZN) microscopy. The other half was expectorated directly into trisodium phosphate-based disinfectant transport medium and on reaching the laboratory 2 drops
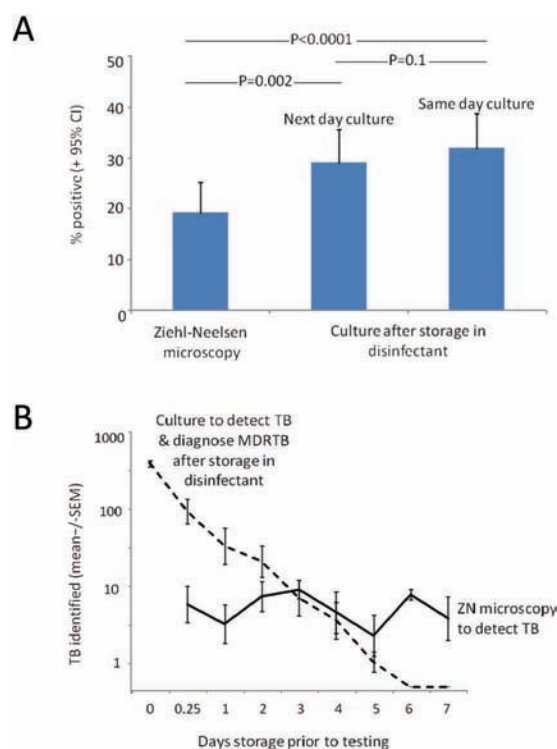
were applied directly to selective 7H11 agar without any processing. After 24 hours storage, another 2 drops were applied to another culture plate. Plates included quadrants with isoniazid and rifampicin for direct susceptibility testing. Subsequently, 6 patients with newly diagnosed smear positive TB provided large volumes of sputum that were cultured after 0–7 days storage in disinfectant. ZN microscopy on neat sputum was done after the same time intervals.

Results: Same day culture detected 70% more TB cases than microscopy (32% vs. 19% positive, $P < 0.0001$). When delayed until the next day, culture remained superior to microscopy (29% vs. 19% positive, $P = 0.002$; graph A). Culture following up to 3 days storage in disinfectant had greater sensitivity than microscopy for diagnosis, while also allowing concurrent resistance testing (graph B). Beyond 3 days, sensitivity for diagnosis dropped to less than that of microscopy.

Conclusions: In-transit sputum disinfection allowed TB culture with concurrent MDR-TB testing using minimal technical skills and equipment. Sputum disinfected in-transit should be processed in the first days after collection; or if prolonged transit is unavoidable then disinfection should be postponed until sputum reaches the laboratory.

PS-100905-14 The diagnosis of pulmonary tuberculosis by concentrating sputum with filtration

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Background: Filtration concentrates TB from sputum, potentially avoiding the expense and biohazard of centrifugation. We characterized the determinants of sputum filtration performance.

Methods: 111 sputum samples (2 ml) underwent standard NALC-NaOH decontamination and were neutralised in PBS. Half of each sample was centrifuged and the pellet cultured in the MODS technique. The other half was aspirated with a syringe through a 25 mm diameter 0.4-μm pore size polycarbonate filter (Millipore) in a reusable holder. Filters were cultured directly in MODS culture broth.

Results: Centrifuge vs. filter-concentration yielded similar sensitivity, colony forming units (CFU), and speed (all $P > 0.2$). This was despite most of the fil-

tration aliquot being discarded because only a median 0.8 ml (IQR 0.2–1.5) of the intended 3.5 ml volume could be aspirated through the filter before blockage. Filterable volume was not associated with microscopy grade ($P = 0.2$) but was influenced by sputum viscosity: median 0.8 ml for salivary/mucoid samples but only 0.2 ml for mucopurulent samples ($P < 0.03$). The volume that could be passed through the filter was not associated with culture speed ($P > 0.1$), CFU that grew on the filter (graph A), or the relative concentrating efficiency of filtration compared with centrifugation (graph B). CFU on the filter was independently associated with ($P < 0.05$) culture speed, CFU in the paired centrifuge-concentrated culture and the microscopy grade but there was no association with ($P > 0.1$) the sputum viscosity.
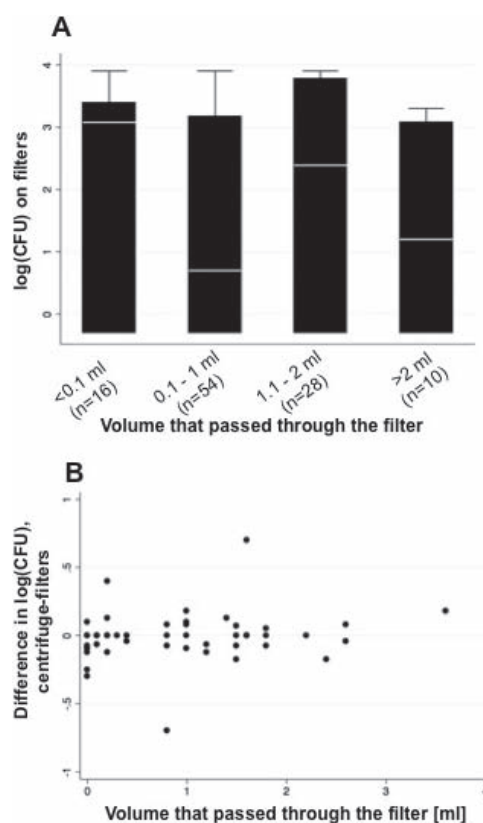
Conclusion: Filtration sensitivity for detecting TB was unrelated to how much sputum would pass through the filter and even when this was <10% of the sample, the sensitivity was similar to centrifuge-concentration. This paradoxical finding implies that filterable volume is not the principal predictor of the efficiency with which filters concentrate TB from sputum.

PS-101017-14   Results and EQA of MODS assay in the first year of universal access to diagnose MDR-TB in Peru

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Background: Three regions in Peru have approved their technical reliability for the MODS and began providing free service for the population: Callao (CA) since Oct 2008, Lima Sur (LS) since Dec 2009 and Arequipa (AQP) since Mar 2009.
Aim: To report the results and quality assurance of MODS in operations conditions in the Peruvian Health Care System.
Methods: The health regions of CA, LS and AQP, the INS and the TB program have launched the universal access to diagnose MDR-TB. Pulmonary samples of all patients with pulmonary TB (smear positive or negative) and before to start treatment, are evaluated by MODS. The results are introduced in NETLAB (Internet based Peruvian Network Lab System). Strains with resistance to isoniazid (H) or rifampicin (R) and 5 to 10% of sensitive are sent to INS for further evaluation in the proportion in agar 7H10 assay for 5 firs and 6 second line drugs. These results also are introduced in NETLAB using the same id-code. Reports of concordance between MODS and APP as a control of quality are made automatically by NET-LAB. We report results until Nov 30th 2009.
Results: The number of MODS tests, positive culture, contamination and TB-MDR results for CA were: 2219, 1212 (55%), 65 (2.9%) and 164 (13.5%); for LS were: 2034, 1415 (70%), 38 (1.9%) and 110 (7.8%); and for AQP were: 315, 233 (74%), 7 (2.2%) and 15 (6.5%), respectively. The mean of time since reception of samples until the publication of MODS results on Internet for CA, LS and AQP was: 17, 14.8, and 24.7days, respectively. Of out 1746 smear negative samples, 322 (18.4%) were detected as positive by MODS culture and 10% of them were MDR-TB. The concordance, sensitivity, and specificity between MODS and APP for H were 90%, 86.2%, and 96.2%, and for R were: 95.6%, 89.7%, and 98.9%, respectively.
Conclusion: In the operations arena, the MODS assay is showing a good performance, inclusive for smear-negative samples and is permitting a rapid diagnosis of TB and MDR-TB simultaneously.

PS-101022-14   The impact of MODS in shortening diagnostic and treatment delays in patients with MDR-TB in Peru

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Background: Rapid diagnosis and treatment of MDR-TB are associated with better clinical outcomes. Three regions in Peru are currently using the MODS assay to rapidly diagnose MDR-TB.
Aim: To determine if the MODS assay shortens the time to diagnose and start treatment among MDR-TB pts.
Methods: We compared the time elapsed in diagnosing MDR-TB and initiating treatment with second line drugs in MDR-TB pts using data from cohorts assembled two years before (group A) and six months after (group B) implementing the MODS assay. Clinical records, lab reports and treatment cards were reviewed in each primary health care center and at the Peruvian Lab Network.
Results: 287 MDR-TB pts in the A group and 86 MDR-TB pts in the B group were evaluated. Mean age of pts in both groups was similar; 30.7 in the A group vs. 32.7 in the B group ($P = 0.41$). Proportion of males and HIV rates did not differ: 63% in A group vs. 62% in B group ($P = 0.86$), and 4% in A group vs. 7% in B group, $P = 0.3$. More primary MDR-TB pts were detected in the B group: 63% vs. 50%. $P = 0.006$. Time to diagnose MDR-TB [mean (SD) and IQR] was shorten in group B vs. group A; 20.6 (8.7) and 12 days vs. 157 (69) and 88 days, $P < 0.001$, respectively. Time to start appropriate MDR-TB treatment was shorten in the B group compared to the A group: 59.8 (31.8) and 33 days vs. 248.6 ± 124 and 128 days, $P < 0.001$, respectively.
Conclusion: The MODS assay improves overall management of MDR-TB pts by shortening the time to diagnose and start appropriate treatment. More primary MDR-TB pts are also detected with the MODS assay. Whether these benefits translate into better clinical outcomes should be further evaluated.

PS-101073-14   Development and findings of an assessment tool for BSL-2 and -3 TB reference laboratories in Nigeria

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Background: The National TB and Leprosy Control Program (NTBLCP) developed a strategy of one na-

tional and six zonal TB reference laboratories to address the MDR/XDR-TB epidemic in Nigeria. A local expert team of FHI which established the first bio-safety-level (BSL)-3 TB laboratory in Nigeria and which included lab scientists, engineers and architects was assigned by the NTBLCP to assess the status of the six zonal TB reference labs.

Methods: An assessment tool for BSL-2 and -3 TB laboratories was developed. It scores in 11 sections the infrastructural, functional and safety status. An example of one section of the assessment tools is shown as attachment. It was applied during visits to each of the zonal TB reference laboratories through observations and structured key informant interviews. Findings were analyzed and reviewed by the whole assessment team.

Results: The overall findings are expressed in mean percent (range percent) of the maximum score: General/administrative requirements 71 (25–100), laboratory finishing and infrastructure 47 (36–60), equipment/supplies 27 (17–30), reagents/media 27 (0–50), bio-safety cabinet 28 (20–30), health/safety 28 (12–45), equipment functions 1 (0–6), performance records 19 (0–57), quality control 9 (0–17), personnel information 8 (8–8) and molecular biology 6 (6–6). Key recommendations for improvement included strengthening laboratory administration; provision of ventilation system, liquid waste neutralization chamber, fire alarm and smoke detectors; standardization of supplies and service contracts; establishment of transport/referral network, development of safety and quality policy, and annual medical surveillance program.

Conclusion: The assessment tool was highly efficient in identifying in a standardized and verifiable way strengths and weaknesses of TB reference labs. The findings have guided decisions of the NTBLCP to further strengthen laboratory systems for MDR/XDR-TB in Nigeria.

PS-100104-14   Direct nitrate reductase assay for drug-resistant TB in smear-positive specimens

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Introduction: Rapid, simple drug susceptibility tests like direct Nitrate Reductase Assay, applicable in developing countries, would allow earlier treatment of patients with multidrug-resistant *Mycobacterium tuberculosis* infections. The objective of the study was to evaluate the performance and feasibility of direct Nitrate Reductase Assay for detecting the drug-resistant tuberculosis directly in microscopy positive samples.

Methods: This prospective study comparing the sensitivity and specificity of the Direct Nitrate Reductase Assay with the gold standard Löwensten-Jensen

proportion method was carried out at National Tuberculosis and SAARC Tuberculosis Reference Laboratory, Thimi, Bhaktapur, Nepal from June 2008 to March 2009. Altogether 302 sputum samples were included for study and 121 sputum samples those showing positive for Acid Fast Bacilli were tested by direct Nitrate Reductase Assay.

Results: The sensitivity and specificity of the Direct Nitrate Reductase Assay were studied in 121 samples and were 100% and 91% for isoniazid, 100% and 98.95% for rifampicin, 96% and 91.66% for streptomycin, and 100% and 98% for ethambutol respectively. Of the 121 samples tested for drug susceptibility, 72.72% (88) were sensitive to all four drugs and 27.28% (33) were resistant to one or more drugs with 19% (23) multidrug-resistant.

Conclusion: The Direct Nitrate Reductase Assay is sensitive and specific enough for the detection of multidrug-resistant tuberculosis and is also easy too perform, rapid and inexpensive, making it suitable for developing countries. However, its usefulness for national drug resistance surveys should be assessed.

PS-100122-14   Anti-tuberculosis drug resistance in the Costa del Sol Health District

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Aim: To determine the rates of resistance to anti-tuberculosis drugs in strains isolated from *M. tuberculosis* in patients treated in the health area of the Costa del Sol District Health.

Methods: In our study we have included a total of 181 patients diagnosed of tuberculosis in the Costa del Sol District Health, during the years 2004 to 2008. The 75.1% (136) come from men and 24.9% (45) of women with a mean age of 40.3 years. The 88.4% (160) had a pulmonary origin remaining 11.6% (21) being extrapulmonary. The number of patients co-infected by HIV was 10 (5.5%) and 64 (35.3%) this data is unknown. All samples are cultured in common culture media and positive cultures were identified. Strains of *M. tuberculosi*s are processed for sensitivity study. The study of sensitivity has been in a total of 168 strains isolated, analyzing susceptibility to first line drugs through the automatic MGIT 960 (Becton-Dickinson) system following the recommendations of the manufacturer.

Results: We have obtained a isolated resistance to INH in 12 strains (7.14%) and to STR in 5 (3.0%). The strains MDR-TB (resistance to INH + RMP) were found 2 (1.2%). Another of the encountered resistance was INH + STR with a total of 1 strain (0.5%). Strains resistant to INH + RMP + STR + ETB were 1 (0.5%) of the total.

Conclusion: The data obtained in our study are similar to those reported in our country. We didn't find different rates of resistance in patients co-infected with HIV than other patients. It is important to study of resistance of *M. tuberculosis* in different areas of health to conduct a proper empirical treatment in the diagnosis of infection.

PS-100698-14   Direct agar proportion method from positive MGIT fluid for drug susceptibility testing

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Aim: BACTEC MGIT 960 system is widespread used for mycobacterial cultures in Taiwan. However, the drug susceptibility testing of positive MGIT 960 still depends on the subsequent subculture on Löwenstein-Jensen medium and indirect agar proportion method, which takes longer time but more cost-saving. The aim of this study is to evaluate the accuracy and turn-around time of the modified agar proportion method by direct using positive MGIT 960 fluid for susceptibility testing of first-line anti-TB drugs.

Methods: After mycobacteria were isolated from clinical specimens by MGIT 960 system, smear for cord formation and MeDiPro *M. tuberculosis* Antigen Rapid Test were used routinely for rapid identification of *M. tuberculosis* at TB laboratory of Taipei Medical University-Wan Fang Hospital. Thereafter, susceptibility testing of *M. tuberculosis* to first-line drugs by modified direct agar proportion method using positive MGIT fluid and conventional indirect agar proportion method using subculture colonies from L-J medium were simultaneously proceeded. Agar proportion method was carried out by inoculating *M. tuberculosis* suspension onto Middlebrook 7H10 agar with drug concentration of 0.2 μg/mL for isoniazid (INH), 1.0 μg/mL for rifampin (RMP), 5 μg/mL for ethambutol (EMB), and 2.0 μg/mL for streptomycin (SM). The turnaround time and drug susceptibility testing results were compared by these two methods.

Results: A total of 432 *M. tuberculosis* isolates were included in this study. The average shortening of turnaround time was 14 days (direct agar proportion method: 36 days vs. conventional indirect agar proportion method: 50 days). The concordance rates between these two methods were high with INH: 98.4%, RMP: 99.3%, EMB: 98.4%, SM: 97.2%, respectively.

Conclusion: This modified direct agar proportion method from positive MGIT fluid for susceptibility testing of *M. tuberculosis* can provide an average of 2-weeks time saving and a good concordance with conventional method.

PS-101042-14   Concordance of drug susceptibility test results for 1st line and 2nd line anti-TB drugs

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Background: The Preserving Effective TB Treatment Study (PETTS) is a multi-country prospective study that aims to determine the frequency of, risk factors for, and consequences of acquired resistance to second-line TB drugs (SLD) in patients with multi-drug-resistant (MDR) TB, defined as TB with resistance to both isoniazid (H) and rifampicin (R). All patients enrolled at TDF had baseline isolates with DST results showing MDR-TB prior to starting SLD treatment. Duplicates of these isolates were sent to CDC's Mycobacteriology Laboratory for re-testing.

Objective: To determine concordance of DST results to H, R, ethambutol (E), pyrazinamide (Z), streptomycin (S), ofloxacin (Ofl) and kanamycin (Kan) between the TDF and CDC laboratories.

Method/design: We compared DST results of 256 patients who had positive baseline cultures (specimens taken within 30 days before or after the start of MDR-TB treatment) and DST results from both TDF and CDC. Both laboratories use the proportion method on Middlebrook 7H10 agar. At CDC, drug powder is dissolved in agar to give concentrations (μg/ml) of H-0.2 and 1.0, R-1.0, E-5.0, S-2.0, Ofl-2.0, and Kan-5.0, while TDF uses Disc Elution with discs calibrated to give these same concentrations. Resistance was defined at a critical proportion of ⩾1% in both labs. For Z, TDF used the Wayne method and CDC used the MGIT 960 method at 100 μg/ml.

Table   Comparative agreement of TDF and CDC DST results

Drug	N	TDF DST Total number of resistant	CDC DST Total number of resistant	Con-cordance Resistant (%)	TDF DST Total number of sensitive	CDC DST Total number of sensitive	Con-cordance Sensitive (%)	Agreement resistant & sensitive (%)
H	255	252	255	98.82	0	0	100.00	98.80
R	256	245	249	98.39	2	7	28.57	97.27
S	255	128	146	87.67	99	109	90.83	85.10
E	254	160	192	83.33	40	62	64.52	78.74
Z	30	11	20	55.00	5	8	62.50	57.14
Kan	251	3	5	60.00	246	246	100.00	99.20
Ofl	99	3	3	100.00	93	96	96.88	96.97

Results: Concordance was 97.3% for R, 98.8% for H, 97.0% for Ofl and 99.2% for Kan. Concordance was substantially lower for S (85.10%), E (78.74%) and Z (57.14%). Compared with CDC's results, the MDR-TB detection rate of TDF was 98.4%.

Conclusion: Our results indicate excellent concordance of DST results for R, H, Ofl and Kan but not S, E and Z. Further development of laboratory procedures to improve DST for the last three drugs is urgently needed, especially for patients with MDR-TB.

PS-101081-14 Potential of the nitrate reductase assay as a potential tool for drug susceptibility testing

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Introduction: Globally Nigeria ranks 4th among the 22 TB high burden Countries. Early detection and treatment of infectious cases reduces the spread of TB while rapid and low cost susceptibility testing of *Mycobacterium tuberculosis* is imperative for treatment monitoring early diagnosis of MDR-TB.

Objective: To evaluate and compare the nitrate reductase assay (NRA) as a potential conventional alternative in vitro drug susceptibility testing which is inexpensive and presents quick results with the proportion method (PM) in our resource poor setting.

Methods: Strains of *M. tuberculosis* which were isolated on LJ slopes from 118 TB patients seen at the National Tuberculosis Reference Laboratory in Lagos, Nigeria in 2009 were tested against four first-line anti-TB drugs by proportion method. In parallel the strains were analyzed by NRA in which the first line drugs were also incorporated. At the end of incubation, reduction of Nitrate was recorded. The results obtained were compared to those obtained by the proportion method in LJ medium containing primary anti-tuberculosis drugs.

Results: In comparing NRA to the proportion method which is the gold standard there was 100% agreement for rifampicin while 98% agreement was recorded for others (isoniazid, ethambutol and streptomycin). Results were obtained in 10–14 days by NRA as compared to PM which were available in 4–7 weeks.

Conclusion: The NRA has shown to be simple, rapid and inexpensive method for TB drug susceptibility testing especially in resource poor setting. It is also a good method for MDR-TB detection.

PS-101112-14 Comparison of MGIT 960, Löwenstein-Jensen and Finn II in Vladimir Oblast Central TB Laboratory

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Objective: To compare 1) MGIT, Löwenstein-Jensen (LJ) and Finn II for recovery of AFB for mycobacterial culture, and 2) MGIT with LJ absolute concentration method (ABS) for drug susceptibility testing (DST).

Methods: A total of 500 specimens (208 patients) were cultured on MGIT, LJ and Finn II. DST to isoniazid (INH), rifampin (RMP) and ethambutol (EMB) were performed in parallel by conventional ABS and MGIT 960 methods. Discordant DST were retested by CTRI using MGIT.

Results: AFB were isolated from 232 specimens (134 patients): 194 (84%)-MGIT, 156 (67%)-Finn II and 88 (38%)-LJ. Combined recovery rates were: MGIT/Finn II-231 (>99%), MGIT/LJ-148 (64%)and LJ/Finn II-172 (74%). Mean time to detection (TTD) for MGIT was 10 days (d) and 34 d for solid media. For DST, the mean time to results after TTD was 15 d for MGIT and 30 d for ABS. DST results were in full agreement for 198 of 215 (92%) isolates for all 3 drugs with both methods and differed for 1 drug in 16 isolates from 9 patients. In these 9 patients, the differences were as follows: MGIT resistant [R]/ABS susceptible [S] for 4 INH, 1 RMP, and 1 EMB; MGIT [S]/ABS [R] for 1 INH and 1 RMP. One isolate was [R] to all drugs by MGIT and [S] by ABS. Upon repeating the DSTs, reproducibility was 100% for all 3 drugs by MGIT, while by ABS it was 94% for INH, 100% for RMP, and 94% for EMB. When 7 isolates with single drug discrepancies were retested by CTRI, results for INH and RMP were in agreement with the original MGIT result while EMB remained discordant.

Conclusion: MGIT in combination with Finn II maximized the yield and decreased TTD compared to the conventional LJ/Finn II combination. DST by MGIT correlated well with the absolute concentration method and provided results in half the time.

PS-100633-14   Reliability of the MODS assay decentralization process in three health regions in Peru

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Background: Rapid tests for isoniazid (H) and rifampicin (R) drug susceptibility testing need to be available close to patients to be useful. We designed a process to decentralize the MODS assay to 3 health regions in Peru.
Aim: To evaluate the reliability of the MODS decentralization process.
Methods: Biologists from each regional laboratory (RL) received MODS training at UPCH. Each RL was asked to process at least 120 sputum samples with MODS (around 80% with smear positive). A post-decontamination back-up of each sample was processed in parallel reference MODS testing at UPCH. The MODS results of regional and UPCH laboratories were sent separately and blinded to the INS where the agreement in culture, drug susceptibility and rate of contamination between UPCH and each RL were evaluated. Pre-determined criteria for successful performance were: concordance for culture and susceptibility to H and R $\geqslant 95\%$, McNemar $P > 0.05$, Kappa index (κ) > 0.75 and contamination between 1–4%.
Results: The number of samples (% of smear positive), processed for Callao, Lima Sur and Arequipa were 126 (79.4%), 130 (84%) and 126 (80%), respectively. The concordance, McNemar P and κ for each RL were Callao: culture (100%, $P = 1.0$, $\kappa = 1.0$), H susceptibility (98%, $P = 1.0$, $\kappa = 0.95$), R susceptibility (97%, $P = 1.0$, $\kappa = 0.91$); Lima Sur: culture (99%, $P = 1.0$, $\kappa = 0.97$), H susceptibility (97%, $P = 1.0$, $\kappa = 0.9$), R susceptibility (95%, $P = 1.0$, $\kappa = 0.81$) and Arequipa: culture (98%, $P = 0.5$, $\kappa = 0.94$), H susceptibility (98%, $P = 0.5$, $\kappa = 0.86$), R susceptibility (97%, $P = 0.25$, $\kappa = 0.75$). Contamination was 1.0–2.3%. The time to complete the decentralization process for Callao, Lima Sur and Arequipa was 94, 97 and 173 days, respectively. Mean MODS processing time for the same RL was 10.7, 9.9 and 12.9 days.
Conclusions: The transference of the MODS assay was reliable and fast. With these results, the INS authorized RL perform the MODS assay. Permanent EQA is ongoing to maintain this performance.

PS-100983-14   Performance of BACTEC MGIT 960 vs. FINN II for recovery of *M. tuberculosis* in Vladimir TB Dispensary

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Methods: The performance of BACTEC MGIT 960 culture system and drug susceptibility testing (DST) to first-line drugs (FLD), Isoniazid (INH), Rifampicin (RMP) and Ethambutol (EMB) was evaluated and compared to FINN II, a recommended medium as second standard medium for mycobacterial culture. Samples were collected between January and November 2009 from new TB cases.
Findings: We analyzed 705 sputum samples were collected and tested on both methods BACTEC MGIT 960 and FINN II between January and November 2009. Among them 44% (310/705) were smear positive. The recovery rates were 88.4% with BACTEC MGIT 960 vs. 82.6% with FINN II from positive smears; while only 56.9% vs. 52.9% of recovery rates were obtained when comparing all smear results. Proportion of concordant results on both MGIT and FINN II was high (88.1%) for smear positive and smear negative results. The proportion of MDR-TB found was similar on MGIT 960 (23.2%) and FINN II (24.5%). There was good concordance between the results obtained by BACTEC and FINN methods with agreement of 94.1% for RMP but only 86.9% for INH, and 79.7% for EMB. The rate of contamination was 4.1% was obtained on MGIT 960 vs. 3.3% on FINN II. Half (50.3%) of strains tested on BACTEC MGIT 960 for were resistant to INH vs. 40.3% on FINN II.
Conclusion: In general BACTEC MGIT 960 system has shown more sensitivity than FINN II for culture of *M. tuberculosis*. The results obtained with FINN II medium were similar with those obtained with Löwenstein-Jensen in other settings. The rate of contamination with BACTEC MGIT was very low (4.1%).

ABSTRACT PRESENTATIONS MONDAY 15 NOVEMBER 2010

FEATURED ABSTRACT PRESENTATIONS

EPIDEMIOLOGY AND CLINICAL RESEARCH IN MDR-TB

FA-100178-15   Adverse drug reactions in XDR-TB patients with and without HIV infection

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Rationale: Significant adverse drug reactions (ADRs) have been reported with second and third line anti-tuberculosis (TB) medications. We describe ADRs during treatment of XDR-TB patients, the majority HIV co-infected.
Methods: Retrospective cohort study of adult patients admitted to a SA public TB referral hospital from December, 2006 to October, 2007; had drug susceptibility testing revealing XDR-TB, and agreed to therapy. ADRs were classified based on clinical impression, audiometry, and lab testing.
Results: 114 XDR-TB patients were treated with a median 5 drugs. 82 (73%) were HIV+, and 50 (61%) were on anti-retroviral therapy (ART). 56 HIV+ patients (68%) had available CD4 counts; median 193 (IQR 85–299). 52 patients (46%) experienced at least 1 ADR or Adverse Event (AE). 29 (25%) experienced a serious ADR, considered severe or life threatening (grade 3 or 4). Among all patients with ADR/AEs the following were found: electrolyte abnormalities (28%), psychosis/confusion (21%), gastrointestinal (19%), hearing loss (13%), seizures (4%), peripheral neuropathy (4%), allergic reaction (4%), acute renal failure (2%), uveitis (2%). Among 23 patients with a serious ADR requiring stopping a medication: Cycloserine (12), Carpeomycin (5), Para-amino Salicylic Acid (2) and Ethambutol (1) were implicated. 5/60 (8%) patient deaths were attributed to ADRs/AE with electrolyte abnormalities (4) and acute renal failure (1) the presumed cause of death.
Discussion: XDR-TB-HIV co-infection is difficult to treat with poor treatment outcomes and survival. It requires a prolonged course of drugs with significant toxicities. We report significant ADRs/AEs causing substantial morbidity and mortality. Treatment of XDR-TB requires close clinical and laboratory monitoring for serious ADRs including electrolyte abnormalities and psychiatric disorders which may be associated with significant morbidity and mortality.

FA-100561-15   Anti-TB regimens based on rifampicin and isoniazid susceptibility: the next step after rapid test

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Background: Current WHO guidelines to treat drug-resistant tuberculosis (DR-TB) recommend implementing rapid tests to evaluate drug susceptibility (DS) to isoniazid (H) and rifampicin (R). However, there is scarce information on which regimens to choose based on these results.
Aim: To elaborate regimens to treat TB based only on DS to H and R.
Methods: We evaluated 13 147 DS to all first and to six second line TB drugs between 2007 and 2009 at the National TB Laboratory in Peru using the proportion method in agar 7H10. DS tests results were classified in 4 groups (G): G1 [H & R sensitive]: 6155 (44.5%); G2 [H resistant & R sensitive]: 1975 (14.3%); G3 [H sensitive & R resistant]: 379 (2.7%), and G4 [H & R resistant (MDR)]: 5321 (38.5%). Following WHO guidelines, we elaborated several possible regimens for each G and evaluated the probabilities (PR) to have 3 and 4 active drugs for G1 to G3, and 4 active drugs for G4. We compared the costs in Peru of these regimens and selected the cheapest one with the best probability of containing active drugs for each G adjusting by age, sex, previous treatment and place of residency.
Results: We selected 5 regimens, two for G2. The regimens and PR to have 3 and 4 active drugs for G1 to G3 and 4 active drugs for G4 were: G1: HRZE (PR = 1.0 and 0.99) G2: REZCfx (PR = 0.99 and 0.86) and REZCfxKm (PR = 0.99 and 0.98) G3: HEZCfxKm (PR = 0.99 and 0.95); and G4: EZCfxKmCsPAS (PR = 0.89), respectively. PR were not modified by age or sex. Previous treatment and place of residency modified PR for G4; the worst case scenario was for previously treated patients living in Lima (Pr = 0.87). HREZ was the cheapest (20.3 US) and EZCfxKmCsPAS the most expensive (1860.4 US) regimen.
Conclusion: It is possible to propose regimens based on DS to H and R that include at least 3 or 4 active drugs with expected high cure rates. These proposed regimens should be further validated under field conditions. New fluoroquinolones must replace Cfx.

FA-100734-15   Risk factors for baseline ofloxacin resistance and XDR-TB among MDR-TB patients in the PETTS study

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Setting: Overall, 483 multidrug-resistant (MDR)-TB patients were treated from February 2005 to September 2008 in Latvia. Of these, 49 cases (10%) had extensively drug-resistant (XDR)-TB. 100 MDR-TB patients were enrolled (2/2005 to 9/2008) in the Preserving Effective TB Treatment Study (PETTS), and 8 of them (8%) had XDR-TB.
Objectives: To determine risk factors for having resistance to ofloxacin (OFL) and XDR-TB for patients in PETTS study.
Methods: Baseline demographic, clinical and laboratory data for 100 patients were entered into standardized database. For each patient, drug susceptibility tests (DSTs) were performed at CDC by the proportion method on Middlebrook 7H10 agar for 12 drugs from specimen taken at the start of treatment. XDR-TB was defined as TB with resistance to at least isoniazid, rifampicin, a fluoroquinolone, and a 2nd-line injectable drug.
Results: Eight patients had XDR-TB, 92 did not. Statistically significant ($P < 0.0001$) risk factors for XDR were: female sex (6/8 vs. 24/92), previous treatment for MDR-TB (5/8 vs. 7/92), and previous treatment with SLDs (7/8 vs. 14/92), specifically injectables (7/8 vs. 11/92), quinolones (6/8 vs. 8/92), and cycloserine (4/8 vs. 11/92). Fourteen patients had OFL resistance. Significant risk factors included female sex (8/14 vs. 22/86, $P = 0.02$), being a health care worker (2/14 vs. 0/86, $P = 0.02$), previous treatment for MDR-TB (6/14 vs. 6/86, $P = 0.001$), and previous treatment with SLDs (9/14 vs. 12/86, $P = 0.0001$), specifically injectables (9/14 vs. 9/86, $P = 0.0001$), quinolones (7/14 vs. 7/86, $P < 0.0001$), and cycloserine (5/14 vs. 3/86, $P = 0.0002$).
Conclusions: Previous use of SLD were risk factors for both OFL resistance and XDR-TB. Females and health care workers were also at increased risk.

FA-101453-15   Association of poor culture conversion with fluoroquinolone resistance in Gujarat, Western India

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Background: India has the world's highest burden of multidrug-resistant tuberculosis (MDR-TB). Programmatic management of MDR-TB began in Gujarat State in 2007. Poor initial microbiological outcomes in the initial cohort prompted an investigation of causes.
Objective: To evaluate interim 12-month outcomes and risk factors for culture conversion among MDR-TB patients treated with a standard 24-month treatment regimen in Gujarat.
Methods: Retrospective cohort study. Clinical and microbiological data were abstracted from registers and treatment cards. Culture conversion was two consecutive negative culture results > 30 days apart. Second-line drug (SLD) susceptibility testing results were provided by a national reference laboratory.
Results: Among 131 MDR-TB patients registered Sept 2007–Dec 2008, fluoroquinolone (FQ) resistance was detected amongst 53 (40%, or 56% of the 95 tested isolates); resistance to FQ and kanamycin (XDR-TB) was uncommon (4 patients, 4%). Overall 84 patients (64%) achieved culture-conversion at any time in the first 12 months, including 5 (4%) who later died or defaulted and 5 (4%) who later reverted to culture-positivity. Seven (5%) died or defaulted without ever culture-converting, and 22 (17%) remained alive and culture-positive for all 12 months. By 12 months, 15 (12%) had died and 14 (11%) had defaulted. Patients with baseline FQ resistance,

Table   Risk factors for culture conversion among MDR-TB patients in Gujarat State, Western India, 2007–2008

Characteristic	Frequency (%) ($n = 131$)	Adjusted Hazard Ratio for culture conversion (95% confidence limits)
Male sex	83 (63)	0.98 (0.61–1.56)
Prior TB treatment episodes >2	88 (67)	0.86 (0.52–1.43)
Body mass index <15	69 (52)	0.70 (0.41–1.17)
Baseline cavitary disease	78 (60)	0.59 (0.36–0.96)*
Missed any 6 doses†	33 (25)	0.57 (0.33–0.99)*
Any ofloxacin resistance	53 (40)	0.54 (0.31–0.94)*
Any kanamycin resistance	5 (4)	0.48 (0.12–2.02)
Any ethionamide resistance	20 (15)	0.71 (0.36–1.43)
Second-line DST unavailable	36 (27)	0.87 (0.49–1.55)

*$P < 0.05$.
†During the intensive phase of treatment, i.e., the initial 6–9 months where an injectable agent is used.

cavitary disease, or missing > 6 doses during intensive phase (initial 6–9 months) were less likely to achieve culture conversion (Table).

Discussion: A very high prevalence of baseline FQ resistance, extent of disease, and adherence appears largely responsible for poor 12-month microbiological outcomes in the first cohort of MDR-TB patients treated using India's standard MDR-TB treatment regimen. If these findings are confirmed from other sites across India, the regimen may require revisiting. Earlier detection through rapid molecular tests and intensified adherence support may also help.

FA-100614-15   Risk factors for primary multidrug-resistant tuberculosis in Kazakhstan, 2003–2008

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Background: While reported tuberculosis (TB) in Kazakhstan is declining, the proportion of patients with antimicrobial resistance remains high. In 2008, 69% of new, adult patients with smear and culture positive pulmonary TB had drug susceptibility test (DST) results available, of whom 21% had multidrug-resistant (MDR) isolates. We describe risk factors for primary MDR-TB to identify patients to prioritize for early diagnostic testing for drug resistance.

Methods: Using the Kazakhstan National Electronic TB Registry, we selected new, adult patients with smear and culture positive pulmonary TB reported from 2003 to 2008. Primary MDR-TB was defined as known anti-tuberculosis drug resistance to at least isoniazid and rifampin at diagnosis in patients with no prior TB treatment. We compared patients with primary MDR-TB to those with pansensitive isolates using epidemiologic, clinical, and demographic factors by logistic regression.

Results: Of 8415 patients with known DST results, 3520 (42%) had isolates resistant to at least one first line agent, and 1247 (15%) were MDR-TB. Statistically significant risk factors for primary MDR-TB were prison exposure (worker or history of incarceration) (aOR: 5.0, 95%CI 1.6, 15.1); concurrent diabetes mellitus (aOR: 1.7, 95%CI 1.2, 2.3); unemployment (aOR: 1.2, 95%CI 1.0, 1.3); male gender (aOR: 1.2, 95%CI 1.1, 1.4); residing in an urban setting (aOR: 1.2, 95%CI 1.0, 1.4); and Kazakh ethnicity (aOR: 1.2, 95%CI 1.1, 1.4). HIV seropositivity was not a risk factor for primary MDR-TB (aOR: 1.6, 95%CI 0.9, 2.8).

Conclusions: Despite high rates of primary resistance among those tested, the majority of new TB patients are treated without DST results. To deliver proper therapy and prevent unnecessary transmission, efforts must be made to test all cases of TB being placed on therapy. Until resources to do this are available, patients with risk factors for primary MDR-TB should be prioritized for testing.

FA-101396-15   Assessing the burden of MDR-TB in Africa

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Introduction: Large gaps in quality-assured, up-to-date, nationally-representative information on the burden of multidrug-resistant tuberculosis (MDR-TB) exist in Africa. In this abstract, available data on drug resistance from African countries are reviewed and the estimated incidence rate of MDR-TB is calculated.

Methods: Data on drug resistance provided to WHO from African countries from 1994 to 2009 were analyzed. The number of MDR-TB cases estimated to have emerged in 2008 was used to calculate incidence rates of MDR-TB. African countries considered were the 46 countries of the WHO African Region. High MDR-TB burden countries are those estimated to have 4000 MDR-TB cases emerging and/or ≥10% of all newly registered TB cases with MDR-TB, as of 2008.

Results: Only 22 countries (48% of countries) have representative data on drug resistance. Of these, only 12 conducted a nationwide survey since 2000; 10 conducted a survey only at subnational level and/or did not repeat it in the past decade. Among African countries, only the Democratic Republic of Congo, Ethiopia, Nigeria and South Africa are high MDR-TB burden countries. A total of 69 000 MDR-TB cases were estimated to have occurred in Africa in 2008 (53 000–110 000). Considering the estimated incidence rate of

Table   Countries in the WHO African region with an estimated total MDR-TB incidence rate of over 10 cases per 100 000 population in 2008; and estimated total MDR-TB incidence rates for India and China in 2008

Country	Estimated total MDR-TB incidence rate per 100 000 population, 2008
Botswana	27.0
South Africa	26.1
Swaziland	23.2
Zimbabwe	19.2
Namibia	17.5
Rwanda	16.3
Mozambique	15.9
Côte d'Ivoire	12.0
Gabon	10.2
India	8.4
China	7.5

MDR-TB (number of MDR-TB cases emerging annually per 100 000 population), several African countries have rates substantially higher than India and China (see Table), the two countries with the highest estimated number of MDR-TB cases emerging annually. **Conclusion:** The high incidence of MDR-TB per capita in Africa largely reflects the background TB incidence rates, which are the highest in the world. High TB incidence is largely explained by high HIV prevalence. The concurrence of HIV and MDR-TB is known to be a very poor prognostic factor in patients. An urgent need exists to measure drug resistance across the African region, particularly in countries without up-to-date, nationally representative data.

FA-100496-15 The molecular epidemiology of multidrug-resistant tuberculosis in the United States, 2004–2008

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Background: Since 2004, multidrug-resistant tuberculosis (MDR-TB) among reported cases in the U.S. has remained low (~1%), however, the proportion of MDR-TB cases that are foreign-born has remained stable at approximately 80%. Consistent with global efforts to enhance drug resistance surveillance, the Centers for Disease Control and Prevention has begun molecular characterization of all MDR-TB isolates in the U.S to describe potential transmission dynamics.
Methods: As part of routine surveillance, drug susceptibility testing and molecular characterization (spoligotyping and MIRU-VNTR) services are available for all reported culture-positive cases in the U.S. MDR-TB genotype clusters were defined as >2 MDR-TB patients (isolates resistant to least isoniazid and rifampin) residing in the same county with identical genotypes reported to CDC from 01/01/04 to 12/31/08. Descriptive analyses were conducted to explore associations between MDR-TB genotype cluster membership and select clinical, demographic and epidemiologic factors.
Results: Of 68 304 reported TB patients, 601 (1.1% of culture-confirmed TB patients) had MDR-TB. Genotyping information was available for 461 (77%) patients, and 197 (43%) were clustered with at least one other MDR-TB patient. MDR-TB was more common among foreign-born individuals, yet cluster membership was more likely among U.S.-born patients (OR:

1.5; 95%CI: 0.9, 2.3). The East-Asian Beijing lineage accounted for 36% of all reported MDR-TB. Patients with East-Asian Beijing strains were 2.9 times more likely to have cluster membership when compared to other lineages.
Conclusion: This is the first comprehensive nationwide analysis exploring the molecular epidemiology of MDR-TB in the U.S. These data suggest that foreign-born persons contribute the largest proportion of reported MDR-TB in the U.S. but are less-likely to cluster with other MDR-TB cases living in the same geographic area, suggesting limited MDR-TB transmission in the U.S.

FA-101141-15 Clusters of multidrug-resistant tuberculosis in Taiwan, 2008–2009

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Aim: To identify transmission of multidrug-resistant tuberculosis (MDR-TB), a molecular surveillance program was implemented in Taiwan as case reporting in 2008–2009.
Methods: Cluster was defined as two cases notified within one year at the same site (i.e. family, hospital, workplace, school, village, etc). Contact investigations were conducted using a structured questionnaire to collected epidemiological information. In the National Tuberculosis Program, all close contacts of the index case must be followed at least 2 years. Genotyping methods, spacer oligonucleotide typing (spoligotyping), mycobacterial interspersed repetitive unit-variable number tandem repeat (MIRU-VNTR) and restricted fragment length polymorphism (RFLP), were used to identify a cluster. Isolates of 45 MDR-TB cases were genotyped.
Results: We identified nine clusters of MDR-TB, two from Eastern Taiwan, three from Northern, two from Central Taiwan, and two from Southern Taiwan. Of the nine episodes, four were household transmission, two workplace, two mixed-type (household and workplace) and one casual contact. The largest cluster notified from Eastern Taiwan is comprised of 15 patients who had epidemiological links (family, relatives, neighbor, colleagues and casual contacts). The second largest cluster reported from Central Taiwan is comprised of seven cases with close contact (family, relatives and colleagues). We found that Beijing genotype was the major causative *M. tuberculosis* in seven episodes (77.8%, 35/45).
Conclusions: Family contact was the main risk factor for the transmission of MDR-TB. For accurate detection of infection source, contact investigation has to be enhanced outside family.

POSTER DISCUSSION SESSIONS

INTEGRATION AND COORDINATION OF TB-HIV SCREENING CARE AND TREATMENT

PC-100310-15 Assessment of implementation of collaborative TB-HIV activities in rural district of KwaZulu-Natal

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Background: This study aims to assess the level of integration of TB-HIV services at facility level and identify constraints related to implementation of collaborative TB-HIV activities.
Methods: Both quantitative and qualitative research methods were used. Routine data from 11 selected facilities in Sisonke district were collected from Jan–Dec 08 and 26 key informants interviews were conducted with provincial, district and facility managers. Ethical clearance was obtained from the University of the Western Cape and written consent forms were signed by all participants.
Results: Total of 4785 clients were newly diagnosed with TB, the uptake of VCT was 83% and the co-infection rate was 61%. Out of 1664 TBHIV co-infected clients, 66% started on CPT and only 16% started on ART. None of HIV patients were screened for IPT. Qualitative results indicates that from program managers and coordinators' perspective, the common identified constraints include lack of leadership, inequitable distribution of funding for TB-HIV programs, lack of joint planning, lack of supervision to ensure that guidelines are being implemented. From facility managers' perspective, the common identified barriers include scope of practice for nurses; structural and physical layout of TB-HIV services and weak referral system clients that lead to loss of clients in the referral process.
Conclusion: The findings of this study suggest that some integration of TB-HIV services is happening with a good uptake of VCT among TB clients. However, the uptake of CPT and ART among TB-HIV co-infected clients is very low and IPT is still not implemented in KZN. Integration of TB-HIV will require strong leadership that addresses unequal funding between TB-HIV programs, revision of scope of practice of nurses to initiate ART at PHC level and reinforce service delivery mechanism and supervision for implementatation of guidelines.

PC-100457-15 Evaluation of integration of TB-HIV surveillance into tuberculosis treatment for children, Ethiopia

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Background: Tuberculosis (TB) is a leading cause of death among children with HIV. Among children with TB disease, early diagnosis and treatment of HIV can decrease mortality. Unfortunately, TB and HIV care are generally not well integrated, and data on HIV infection in children with TB disease (TB-HIV) are lacking. In 2008, Ethiopia integrated HIV testing variables into its TB treatment registers. We evaluated the impact of the current integrated register on documented HIV testing and assessed how the planned health management information system (HMIS) would impact pediatric TB-HIV surveillance data.
Methods: From the 11 medium and large TB clinics in three regions, we extracted data for children (aged <15 years) diagnosed with TB during September 2007–September 2009. We compared percentages of children with documented HIV test results in preintegration registers (separate for TB treatment and HIV testing) and postintegration registers (combined). We also interviewed hospital staff about TB-HIV integration and about the HMIS.
Results: In preintegration registers, HIV test results by clinic ranged from 0%–82% complete (median 48%, interquartile range [IQR] 24, 71); integrated registers were 86%–100% complete (median 96%, IQR 93, 100). Of 383 children with test results in the postintegration registers, 26 (7%; range 0%–33%) tested positive for HIV. All six staff members interviewed said that the integrated register facilitated recording of HIV data but that the HMIS will not report data separately on children and adults.
Conclusions: Integrating recording of HIV test results into TB registers led to consistently complete data and assurance of HIV testing. To ensure accurate surveillance of HIV among children with TB in Ethiopia, the HMIS should report TB-HIV data separately for children.

PC-100668-15 Successful integration of tuberculosis and HIV care in prisons, Thailand

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Setting: Large prison in Nonthaburi Province.
Objectives: To assess rates of HIV testing and HIV care for TB patients.
Method: TB patients registered between October 2004 and September 2008 were enrolled. All patients were

provided provider-initiated HIV testing and counseling (PITC) by prison nurses. TB patients with HIV infection received HIV related care inside prison health care system and collaborate with local hospital.

Results: Of the 415 TB patients, 99.74% agreed to be tested for HIV infection. The HIV testing rates of TB patients increased from 98.97% in 2004 to 100 in 2008. HIV Prevalence from 2004 to 2008 was 26.20%, 21.65%, 18.90 and 14.40%, respectively. During four years, 82.35% (70/85) of HIV positive patients received cotrimoxazole preventive therapy and 77.64% (66/85) for ART during TB treatment. Success rate from 2004 to 2008 was 89.34%, 94.85%, 95.28% and 100% respectively.

Conclusion: HIV services for TB patients in Thai prisons have been improved by the prison health care system at the central level and more collaboration with local health authorities are integrated HIV services for TB patients in provincial prisons where HIV services depend on local hospitals. This integrated TB-HIV treatment program resulted in excellent adherence and TB and HIV outcomes.

PC-100785-15   One-stop shopping: TB and HIV integrated care in Rwanda

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Background: Rwanda has a high burden of HIV and Tuberculosis (TB). In 2005, the Ministry of Health (MOH) in collaboration with key stakeholders drafted and approved a national policy on TB-HIV including provider initiated HIV testing of all TB patients and enrolment into HIV care for those found to be infected through a one-stop service approach at the TB service. We describe the Rwandan experience in scaling up this one-stop service model nationwide.

Methods: In 2005, the MOH in collaboration with the International Centre for HIV Care and Treatment Programs in Rwanda establish two model centers implementing a one-stop service approach for TB patients with HIV. The model includes systematic HIV testing of TB patients, enrollment into HIV care at the TB service, CD4 count testing, provision of cotrimoxazole preventive therapy (CPT) and antiretroviral therapy (ART) under direct observation. Home visits are conducted for TB contact tracing as well as HIV testing of family members. After completion of TB treatment the patient is accompanied and transferred to the HIV clinic for further follow up. By the end of 2007, the 2 models centers functioned as practical trainings sites. Health care workers from TB services nationwide attended 2 days on the job training after receiving theoretical training on HIV care and

treatment. The MOH in collaboration with partner Institutions ensured regular supervision and site support to assure quality of the TB-HIV integrated services.

Results: By April 2009, 153 of 192 TB diagnostic and treatment centers fully implemented the one-stop TB-HIV service. HIV testing and counseling of TB patients increased from 46% in 2004 to 97% by 2009. The prevalence of HIV among those tested was 34%. Of the HIV-infected TB patients, 92% initiated CPT and all eligible patients were receiving ART.

Conclusion: The Rwandan experience demonstrates that it is feasible to achieve rapid and successful implementation of one-stop TB-HIV services.

PC-100884-15   Institutional challenges and barriers to effective TB-HIV responses

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Background: In many countries with generalized HIV epidemics, rates of TB-HIV co-infection have risen dramatically, pushing down TB success rates and contributing to mortality in HIV+ patients. Recognizing the severity of this problem most high-burden countries have established TB-HIV coordination mechanisms. However, attempts to develop concerted actions to stem both epidemics and to address the needs of co-infected patients have encountered certain challenges. Our research explored how TB and AIDS programs interact and how this interaction affects the response to TB-HIV.

Methodology: Together with local research institutions, we conducted case studies in Burkina Faso and Malawi. We collected data through documentation analysis and interviews with a wide range of stakeholders. Data were analyzed using a framework derived from the SYSRA methodology.

Results: In both countries, TB and AIDS programs have acknowledged the need for effective collaboration. However, we found several barriers at the national and implementation levels. The programs have developed in parallel with distinct organizational set-ups, influencing opportunities and willingness for interaction. For instance, AIDS programs are governed multi-sectorally and benefit from higher level government commitment and greater resources than TB programs, which affects power relationships. Distinct financing sources and protectiveness over earmarked resources complicate collaborations. Individual systems for data collection and supervision limit the exchange of information between services. Different degrees of decentralization of DOTS and ART hinder referral of co-infected patients and add to the burden on patients, increasing the risk of loss from follow-up.

Conclusions: We conclude that more pro-active collaboration by TB and HIV stakeholders is still much needed. This should include breaking down some of

the institutional barriers to collaboration stemming from highly parallel programmatic approaches

PC-101102-15   Global Fund support to TB-HIV collaborative activities in Round 9

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Background: At its 18th meeting in New Delhi, India, the Global Fund Board recognized that the slow process in implementing core TB-HIV collaborative services is a risk to achieving successful outcomes under current and future Global Fund (GF) tuberculosis and HIV grants. The Board emphasized that all applicants should include and implement significant, robust tuberculosis (TB) interventions in their HIV/AIDS proposals, and HIV/AIDS interventions in their TB proposals. This study evaluate the progress related to the Board guidance, by compiling and analyzing the incorporation of TB-HIV in all HIV and TB proposals from Round 9, and compare it with the TB-HIV burden.
Methods: All the TB and the HIV proposals received by the Global Fund in Round 9, were analyzed to evaluate the proportion of funds dedicated to the TB-HIV activities.
Results: Of the 54 TB proposals received by the Global Fund, 85% included TB-HIV collaborative activities. 88% of those recommended by the Technical Review Panel (TRP) included TB-HIV activities. The funds requested represent 3.1% of the total amount approved for funding by the GF Board. Of the 73 countries that applied for funding for HIV programmes, 85% included TB-HIV collaborative activities. 34% of those recommended by the TRP included TB-HIV activities. The funds requested represent 0.9% of the total amount approved for funding by the GF Board.
Conclusions and recommendations: The results suggest that the percentage of approved proposals including a TB-HIV component is low. Furthermore, the total amount of proposals including a TB-HIV activity represents only a small percentage of the total funding for TB and HIV programs.

PC-101267-15   A community VCT model for integrated TB and HIV testing

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Background: The majority of South Africans do not know their HIV status and despite government efforts to scale up access to counseling and testing, most testing is done in health settings with only 34% of those tested being male.

Aim: To increase access to integrated TB and HIV counseling and testing in communities.
Method: Nine Community VCT centres have been established in partnership with non-governmental organizations in high TB-HIV burden communities in Cape Town. This model uses outreach activities to reach clients and targets 'well people' with a special emphasis on males who typically don't access health facilities. Outreach activities are conducted from tents and caravans that are set up at community organizations, commuter interchanges, farms and industries. All clients were tested for HIV and screened for TB according to national guidelines.
Results: 34 861 clients (47% male) attended the community VCT centres from January 2008 to December 2009. 33 175 (95%) received an HIV test, of which 2961 (9%) tested HIV-positive. 3939 (11%) clients had TB symptoms—twice as many HIV-infected clients had symptoms than HIV-uninfected clients. 3223 (82%) clients had TB tests done, with 136 (4%) diagnosed with TB. All were referred for TB treatment and 111 (82%) were confirmed to have started treatment.
Conclusion: This community VCT model has successfully increased access to integrated HIV and TB testing especially for males. 9% of 'well people' were HIV-infected and routine integrated screening for TB resulted in a substantial number of TB cases being diagnosed.

PC-101420-15   TB-HIV collaboration, response from a high-burden setting for both epidemics

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Background: Namibia has an HIV prevalence of 17.8% and a TB case notification rate of 634/ 100 000. HIV prevalence in TB patients was 57.6%. Due to the large co infection rate the government has made strides in ensuring collaborative activities for the response to HIV and TB.
Interventions: A new Directorate of Special Programmes (DSP) was created in 2004 to spearhead the collaboration, headed by a director to whom the chief medical officers in charge of both programmes report. Policy development and strategic planning are managed at this level. The plans for both the TB and HIV control programmes share the same TB-HIV sections, made after extensive cross–consultation. A TB-HIV working group was set up, which meets monthly and deliberates on collaborative activities, policy implications and M&E. Human resources at regional and district level reflect this collaboration with regional, district special programme TB-HIV officers and TB-HIV doctors in hospitals. All cases enrolled in HIV care are offered TB screening using a tool to decide whether to offer IPT or refer for full

TB investigation. A TB infection control (TBIC) policy has been developed. An architect and a TBIC officer have been recruited to address TBIC issues. All TB patients are offered HIV testing routinely. Prevention education and condoms are available in all TB clinics. Cotrimoxazole is given to all TB patients with HIV. HAART is offered according to national guidelines.

Results: Due to the DSP, HIV testing among TB patients has increased from 16% in 2005 to 73% in 2009. Cotrimoxazole coverage among TB-HIV patients was 92% in 2009 while the national ART coverage for those eligible is 88% and 35% of those co-infected in 2009 were on ART.

Conclusions: Successful collaboration of TB and HIV is best coordinated by national body. Care providers should be fully cross-trained in TB and HIV to maximise collaboration in other sectors (eg prisons), an area which is not yet fully addressed in Namibia.
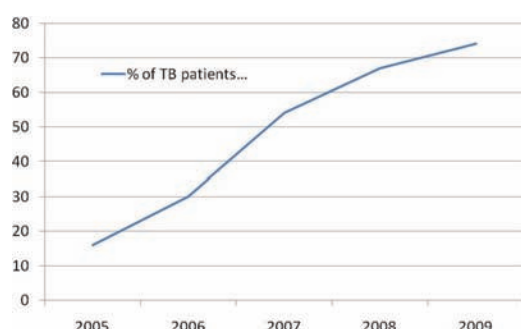

Figure Namibia TB-HIV collaboration: HIV testing among TB patients, 2005–2009.

TB-HIV: COUNSELLING/TESTING/ MONITORING/EVALUATION

PC-100193-15   Monitoring and evaluation system strengthening for TB-HIV control program in the workplace

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Background: For workplace TB-HIV control activities, National TB Program (Bureau of TB-BTB) needs to work with the right team with all stakeholders including National AIDS Program, Thailand Business Coalition on AIDS (TBCA), Local NGOs, private practitioners, community groups, and employers. Monitoring and Evaluation plans have been implemented to improve the program activities.

Intervention: During the two years implementation, BTB & TBCA has raised the key important activities as such 'Recognize that TB is a workplace issue', 'Ensure non-discrimination', 'Respect confidentiality', 'Implement DOTS', 'Work with National TB Program', 'Develop a network of TB program partners', 'Link existing workplace HIV program to new TB program.' The network coordination between government and non-government organization to accelerate TB-HIV and DOTS and monitoring and evaluation in the target areas has been strengthened and promoted.

Lessons learnt: In 2007–2009, BTB & TBCA has implemented and expanded DOTS program and introduced TB-HIV control activities to 4000 companies. 3400 managers and 76 000 employees were directly trained and learned about TB general information by using standards curriculum. Additionally, 28 local NGOs were introduced to TB-HIV control program, 400 TB cases while registered in private hospitals were directly supervised during the treatment course using telephone peer support after the end of working day.

Conclusions: This workplace TB-HIV control should be applied for preventing TB in all enterprises. Providing monitoring and evaluation program on controlling TB among TB-HIV patients, employers, employees and high risk groups in need is very crucial for key success in the future.

PC-100300-15   Routine provider-initiated HIV counselling and testing of adult TB patients in Myanmar

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Background: The Integrated HIV Care program for Tuberculosis patients and their family started in May 2005 in Mandalay. It uses the National TB Program as en entry door for HIV diagnosis and treatment. Provider-initiated HIV counseling and testing (PICT) is offered to all registered adult TB patients and the spouses/children of TB-HIV co-infected patients.

Methods: Number/percentage of patients offered HIV test, tested for HIV, HIV-infected, number/percentage of spouses/children offered HIV test, tested for HIV, HIV-infected, TB disease classification, and number/percentage of HIV-infected patients enrolled, and their outcome were reviewed.

Results: In 2009, 2991 adult TB patients were registered, 2830 (95%) were offered HIV test, 2610 (87%) were tested for HIV, and 803 (31%) were diagnosed

HIV-infected. TB disease was pulmonary sputum smear positive: 248 (31%), sputum smear negative: 416 (52%), and extra-pulmonary TB: 139 (17%). HIV test was offered to 499 spouses/children, 430 (86%) were tested and 263 (61%) were diagnosed HIV-infected. Seventy eight percent of patients were enrolled in the program, among whom 65% were put on ART. The main reason for non enrolment is residency outside of the selected area (64%).

Conclusion: PICT has become routine in these townships and has a high acceptance rate among TB patients. About a third of tested TB patients are HIV co-infected. Most of the TB-HIV co-infected patients are AFB sputum smear negative. Acceptance rate of HIV test among spouses/children is also high and about two third are HIV infected. PICT for TB patients should be expanded as well areas providing ART.

PC-100488-15   TB-HIV household counselling: the route to delivery of isoniazid preventive therapy in Zambia

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Setting: The WHO policy recommends the use of isoniazid preventive therapy (IPT) for people living with HIV. Zambia has adopted other aspects of the TB-HIV policy but does not currently support the use of IPT.In April 2008, Zambian Ministry of Health and ZAMBART (Zambia AIDS Related TB Project) agreed to pilot IPT in 16 ZAMSTAR (Zambia South Africa TB AIDS Reduction Study) sites.

Objective: To review the implementation of IPT through a TB-HIV household counseling intervention in Zambia.

Methods: IPT was implemented in 16 clinics comprising a catchment population of 900 000 people. Eight out of the 16 clinics also had a household counseling intervention which used TB patients as entry point to TB-HIV eductation,screening, testing, IPT and adherence support. ZAMBART and the NTP developed IPT guidelines and registers. Trained health workers did TB screening, administered IPT and monitored clients monthly. Only asymptomatic HIV positive adults, not yet eligible for ART and children <5 with positive TB household contact, got isoniazid daily for 6 months.

Results: A total of 2329 clients, including 15% children, were recruited on IPT. 54% were recruited from the 8 household sites that were also more associated with the recruitment of children (OR5.5, CI 4.10–7.41). The treatment completion rates to date are 75% for Household and 80% for non-Household sites.

Discussion: The introduction of IPT in households created increased access to IPT in children, but not in adults, as most of them were eligible for ART. The treatment outcomes were good in all sites.

Table   IPT recruitments in ZAMSTAR sites, 2008–2009

Quarter/year	Household sites		Non-household sites	
	Adults	Children	Adults	Children
Qtr2 2008	202	37	175	19
Qtr3 2008	124	14	234	14
Qtr4 2008	170	64	206	9
Qtr1 2009	304	92	183	13
Qtr2 2009	166	96	205	2
Total	966	303	1003	57

PC-100820-15   Implementation of monitoring and evaluation system for TB screening in HIV-infected people in Rwanda

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Background: The Ministry of Health (MOH) has been implementing TB-HIV collaborative activities since the scourge of the TB-HIV syndemic in 2005. A national policy was approved including TB screening of people living with HIV (PLWH). Harmonizing and integrating national standardized indicators on TB screening between all stakeholders has been a challenge. The MOH has identified the integration of these indicators in the national telephone based HIV reporting system (TRACnet) as a priority.

Methods: The national TB-HIV working group developed standardized indicators on TB screening for patients newly enrolled in HIV care and treatment (HCT) and for those in follow up. HIV data collecting and reporting tools (HIV patient dossiers, (pre-) ART registers and reporting template) were developed to include data on TB screening, diagnosis and treatment. Partner institutions were trained and started implementation at 24 HCT sites in 2006. Onsite training and site support was conducted at an additional 115 sites in 2007/2008 and the remaining 71 sites in 2009. The initial paper based system has recently been integrated in TRACnet. A broader refresher training on TB-HIV M&E will be organized at district level during the third quarter of 2010.

Results: By the end of the 2nd quarter of 2009, 190 (90%) of HCT clinics in Rwanda regularly reported on TB screening in newly enrolled patients; 168 (80%) reported on patients in follow up. From

1/1/2009–30/6/2009, of 13 460 PLWHA newly enrolled in HIV care at 190 HCT sites, 12 152 (90%) underwent TB screening at enrollment, of these 377 (3%) were diagnosed with active TB disease and started TB treatment. Of 80 344 patients enrolled into care and who are still in the program at 180 sites on 30/6/2009, 50 683 (63%) were screened for TB at least once between 1/1/2009 and 30/6/2009, 489 (10%) had active TB disease and started TB treatment.

Conclusion: Implementation of national integrated system for TB screening of PLWH is feasible.

PC-100853-15   Integrating home based HIV counselling and testing into TB-HIV collaborative activities

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Aim: To describe a successful model in Swaziland of TB-HIV collaborative activities where home based HIV testing and counseling (HTC) using co-infected TB, HIV positive as index case.

Methods: Initially, TB patients who are HIV positive, bedridden and on anti-TB injections at the TB centre in the Manzini region Swaziland, were followed up in their homes by a home based care (HBC) team from the TB centre who administered their injections. HTC and TB screening of contacts was introduced as part of this package. Measurements during the intervention included acceptance of these services as measured by the proportion of family members who accepted an HIV test and number of family members who were screened for TB using a standard TB screening tool. 27 (16 females, 11 males) patients were enrolled into the HBC program and were followed up in 7 communities in the Manzini region by daily home visits. HTC, TB screening of contacts, HIV/AIDS education including condom education were conducted.

Results: Of the 27 families with index TB HIV co-infected patients, 66 family members were reached with HTC and a 100% of those reached accepted HTC. 16, 24% (16/66) tested HIV positive. CD4 samples were collected and sent to the laboratory. 106 family members were screened for TB, including 96 adults and 10 children less than 5 years. 9 (90%) of the children screened positive and referred to the TB centre for further investigations. 80 (83%) adults screened positive for TB, spot sputum specimen were done and another sample was collected on subsequent visits and sent for diagnosis at the TB centre.

Conclusion: The approach demonstrated increased access and acceptability and need to scale up.

PC-100885-15   Intensified TB case finding among HIV-infected patients: lessons learnt from South Africa

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Background: Routine screening of HIV-infected patients for symptoms of tuberculosis (TB) at every clinical visit plays an important role in improving patient outcomes, reducing transmission of TB as well as evaluating patients for eligibility for isoniazid preventive therapy (IPT). Challenges affecting routine TB screening in the Eastern Cape Province of South Africa include the unavailability of a standardized TB screening questionnaire and poor recording of screening outcomes and further management of patients suspected of having active TB.

Intervention: To facilitate routine TB screening and diagnosis of TB among adults in HIV care and treatment, a six question TB screening questionnaire was integrated into a new comprehensive HIV Adult Clinical Record (ACR) that was developed in collaboration with the Eastern Cape Department of Health (ECDOH) and several NGOs. Tools for data abstraction from the ACR into the routinely used HIV care and treatment registers were developed, and an electronic version of the record, linking it with the District Health Information System database, piloted.

Results and lessons learnt: Following introduction of the ACR at 13 HIV care and treatment facilities in a deep rural sub-district in the Eastern Cape, providers were more apt to use the screening questionnaire consistently and to record TB data in a standardized fashion. During 2009, mean proportion of new patients screened for TB at enrollment across 13 sites increased from 54.8% in quarter (Q)1 to 77.0% in Q4 (P for trend = 0.0006), and mean proportion of new patients diagnosed with TB increased from 2.5% in Q1 to 5.8% in Q4 (P = 0.0478) (see Table).

Conclusions: A comprehensive HIV clinical record, integrating a TB screening questionnaire with routine HIV care, can improve TB case finding, as well as facilitate monitoring and evaluation of the TB screening process in HIV-infected patients.

	Jan–Mar 2009	Apr–Jun 2009	Jul–Sep 2009	Oct–Dec 2009
# new HIV patients (pts)	1154	944	930	905
% new pts. on TB treatment at enrollment	11.8% (0%–25.0%) (ref)	11.8% (3.2%–21.6%) (P = 0.8073)	13.0% (0%–28.6%) (P = 0.9986)	16.4% (0%–40%) (P = 0.4476)
% new pts. without TB at enrollment screened for TB	54.8% (25.6%–100%) (ref)	66.6% (18.9%–100%) (P = 0.1170)	69.4% (43.0%–100%) (P = 0.0604)	77.0% (32.4%–100%) (P = 0.0006)
% new pts. diagnosed with TB	1.9% (0%–3.9%) (ref)	3.0% (0%–8.3%) (P = 0.1293)	4.1% (0%–11.9%) (P = 0.0331)	5.6% (0%–18/8%) (P = 0.0478)

PC-100926-15   Using voluntary counselling and testing data to estimate the prevalence of tuberculosis among first-time testers

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Background and challenges to implementation: Voluntary counselling and testing for HIV/AIDS serves as the entry point into care at MU. The World Health Organisation recommends TB screening for all HIV patients because between 50–60% TB patients are co-infected with HIV. From 2004, MU started an intensified TB screening for all individuals that seek services at the clinic. Previously it was difficult to identify clients who needed TB treatment before initiation of other clinical activities that patients required.

Intervention: Upon reporting at the VCT clinic, clients are given pre-test counseling and TB related history is taken. Clients are asked about having had cough for 2–3 weeks, sweating at night and coughing up of blood. All suspected cases provide sputum samples that are confirmed in the laboratory and other cases are sent for chest X-ray. All data is collected and routinely analysed for clinical trends and characteristics.

Results and lessons learnt: From October 2008–December 2009, 1731 clients were screened out of which 165 (9.5%) were detected and treated for TB. Acceptance rates for TB screening are at 100% and initiation into care for all TB confirmed cases is easy.

Conclusions: Institutions that provide HIV/AIDS care should integrate TB testing for all first time testers. This could reduce TB transmission and improve adherence due to low pill burden (since majority of VCT clients are not eligible for ART at the time of HIV testing) and hence decrease mortality due to late TB diagnosis and adverse events related to drug interactions between anti TB drugs and ARVs.

PC-101360-15   Routine data from the Tanzanian TB-HIV programs show high rates of VCT among TB patients but relatively low rates of ART enrollment and ART initiation

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Background: Collaborative TB-HIV activities in Tanzania started in 2005 at 11 sites. To date, all HIV care and treatment clinics (CTC) in Tanzania provide TB screening and referral: 1230 TB clinics provide HIV testing and TB treatment and about 700 HIV clinics offer TB screening, cotrimoxazole preventive treatment (CPT) and Anti Retroviral Treatment (ART).

Methods: Routine data from 2007–8 were reviewed.
Results: Among 62 092 TB cases registered in year 2007, 50% accepted HIV testing and among them 47% tested HIV positive; 67% were registered at HIV clinic, 31% started ART and 72% cotrimoxazole prophylaxis. During year 2008, a similar number of TB cases were notified (63 364), while 77% were offered HIV testing, 41% tested positive; 73% were registered at HIV clinic, 30% were started on ART within 3 months and 82% on cotrimoxazole.
Conclusions: Although a higher proportion of TB patients were tested for HIV in year 2008, the proportion of those who tested positive remained stable over time and shows a high TB-HIV co-infection rate. The proportion of TB-HIV patients who were initiated on ART remained lower than expected over the two years which suggests that there are significant barriers to enrolling ART-eligible TB patients onto ART. These may be related to lack of timely CD4 testing and clinician reluctance to start ART while TB medication is ongoing.

	2007		2008		% Change
	Cases	% of Cases	Cases	% of cases	
TB Cases registered	62,092		63,364		2.0
-TB cases tested for HIV	31,305	50.4	48,846	77.1	56.0
-TB cases tested HIV positive	14,669	46.9	19,940	40.8	35.9
-TB/HIV cases referred to CTC	14,054	95.8	18,980	95.2	35.1
-TB/HIV cases registered for HIV care	9,966	67.9	14,574	73.1	46.2
-TB/HIV cases started ART	4,619	31.5	5,918	29.7	28.1
-TB/HIV cases started CPT	10,541	71.9	16,400	82.2	55.6

PC-101377-15   Outcomes of five years (2004–2009) of antiretroviral treatment for HIVAIDS in Tanzania

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Background: Tanzania, aiming at placing 440 000 HIV+ persons on treatment for HIVAIDS by 2009, has established services in 909 health facilities. TB patients are routinely tested for HIV. Since 2004 growing numbers of patients have been placed on anti-retroviral therapy.

Methods: Data are collected using paper based and electronic, anonymized, data extracted from patient records. We used electronic patient-level data from 88 875 adult patients (age 15 years or more), and 7324 children (aged 0–14 years) initiating ART, from 2004 through to the end of 2009 collected from 101

facilities to monitor outputs and to assess impact of treatment. From 1.2 million visits, hazard rates were calculated and Kaplan-Meier survival graphs drawn. Hazard ratios (HR) and 95% confidence intervals (95%CI) are used to compare groups.

Results: By combining data from paper-based and electronic patient reports an estimated 150 000 to 200 000 patients are currently receiving ART. This represents 63% to 83% of those in need of ART. Two thirds of patients starting ART are female. Cumulative probability of mortality in the 1st year was 10% with worse survival in males (HR = 1.54, 95%CI 1.47–1.61), those with an initial weight under 45 kgs (HR = 3.17, 95%CI 3.00–3.35), and with an initial CD4 count less than 50 cells/ml (HR = 2.19, 95%CI 2.08–2.67). TB screening was recorded at 98.3% of visits, with TB suspected in 5.5% of visits, based on one or more of the screening questions positive. However, the incidence of confirmed TB was higher in the first year on ART (1% of patients). In subsequent years confirmed TB was found in 0.3% of patients per year.

Discussion: Despite the success of the care and treatment programme in Tanzania, inequalities exist. More effort is needed to provide services in those regions of greatest need. There is also a need to improve data reported, to ensure prompt, accurate and complete reports are made to NACP.

TUBERCULOSIS BASIC SCIENCE

PC-100129-15   Daily (7 days a week) versus 5 days a week treatment of TB in immune-competent and -deficient mice

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Aim: Directly observed treatment (DOT) of tuberculosis is often administered 5 days a week (5/7) rather than 7 days a week (7/7) even in patients with immune deficiency. Several authors have claimed that 5/7 treatment is less active than a real 7/7 treatment. We addressed this issue in immune-competent (BALB/C) and immune-deficient (athymic nu/nu) mice infected with *M. tuberculosis*.

Methods: 45 BALB/C mice and 45 nu/nu mice were aerosol infected with 4.5 log10 of *M. tuberculosis*. Oral treatment was initiated 2 weeks later with a 4-drug (in mg/kg) regimen of rifampin (R)10, isoniazid (H) 10, pyrazinamide (Z) 150, and ethambutol (E) 100 for 8 weeks followed with RH. Treatment was given either 7/7 or 5/7. Lungs CFU counts were at done the day after infection, on initiation and after 1, 2 and 3 months of treatment.

Results: At treatment initiation the lung log10 CFU counts were 7.72 ± 0.07 and 7.83 ± 0.13 in BALB/C and nu/nu mice, respectively. They were 0.5 log10 and ~1 log10 lower in 7/7 than in 5/7 treated BALB/C and nu/nu mice after 1 and 2–3 months of treatment, respectively At each time point, the CFU counts were ~1.5 log10 lower in BALB/C than in nu/nu mice.

Conclusion: 7/7 treament is significantly more bactericidal than 5/7 treatment. Response to treatment is much better in immune-competent than in immune-deficient mice.

PC-100702-15   Clinical value of IS*6110*-based LAMP assay for direct detection of *Mycobacterium tuberculosis* complex

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Aim: To achieve the global targets in tuberculosis control, efforts must be continued for the development of novel diagnostic methods. The promising preliminary results of our recently developed IS*6110*-based loop-mediated isothermal amplification (IS*6110*-LAMP) assay (Aryan, E. et al. Microiol Res 2010; 165: 211–220) encouraged us in performing the present study, which aimed to evaluate the clinical performance of this assay on respiratory specimens in comparison with Amplicor MTB and in-house IS*6110*-based PCR and nested PCR tests.

Methods: In this cross-sectional study, a total of 101 sputum samples were randomly collected from 93 highly suspected tuberculosis patients.

Results: Respectively, 3 and 74 sputum samples were confirmed as tuberculosis cases clinically and by culture. The remaining 24 patients were ruled out having tuberculosis according to the patient's clinical follow up. The overall sensitivies of IS*6110*-LAMP, -PCR, -nested PCR, and Amplicor MTB test for diagnosis of pulmonary tuberculosis were respectively of 89.6% (69/77; 95% confidence interval [CI], 80.5–95.4%), 59.7% (46/77; CI, 47.9–70.8%), 79.2% (61/77; CI, 68.5–87.6%), and 76.6% (59/77; CI, 65.6–85.5%). The specificity of the tests was 100%. The overall agreements between LAMP and Amplicor (kappa = 0.88), and between LAMP and nested PCR (kappa = 0.92) were almost perfect, and it was good between LAMP and PCR (kappa = 0.77).

LAMP had more tolerance to inhibitors in clinical samples than Amplicor (2 vs. 7 inhibited reactions, respectively), but this difference was not significant ($P = 0.0625$).

Conclusion: Better diagnostic performance of IS*6110*-LAMP assay than Amplicor ($P = 0.0094$), nested PCR ($P = 0.0133$) and PCR ($P < 0.0001$) tests, in addition to its cost-effectiveness, rapidity and simplicity could make it a valuable diagnostic tool in clinical settings, especially in resource-limited countries.

PC-101259-15   Our experience in use of nitrate reductase assay for rapid susceptibility testing of *M. tuberculosis*

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Aim: Review the results of use NRA for the rapid susceptibility testing of *M. tuberculosis* to five drugs of first-line and to four drugs of second-line obtained in our laboratory during 2002–2009.
Methods: Critical concentrations of the drugs were as follows: INH 1.0 μg/ml, RMP 40 μg/ml, SM 10 μg/ml, EMB 2 μg/ml, PZA 1000 μg/ml, OFX 2.0 μg/ml, KM, AK and CM 30 μg/ml.
Results: Comparable results were obtained with the following interpretation of the NRA results, a strain was considered resistant if any colour change was observed in the drug containing vial. In the drug-free control tube the colour change was no less than 3+. An excellent agreement between NRA and reference methods (the absolute concentration method, the proportion method on Middlebrook 7H10 agar, the automatic system BACTEC MGIT 960) was observed. Good agreement was observed between the NRA and the BACTEC MGIT for PZA. Results for OFX, KM, AK and CM were also promising.
Conclusion: NRA is a diagnostic tool for the rapid detection of *M. tuberculosis* resistance to first- and second-line drugs including PZA. Our study showed a possibility of testing of both MDR- and XDR-TB cases. Further studies are needed to optimize the testing of second-line drugs.

PC-101359-15   Current state of tuberculosis detection using African giant rats (*Cricetomys gambianus*) in Tanzania

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Background: Tuberculosis (TB) is a major public health problem in developing countries. Trained African giant pouched rats (*Cricetomys gambianus*) are reported to have the potential to enhance TB diagnosis capacity in resource-limited areas by olfactory detection. We report on the current state of the TB diagnosis using rats and the detection of TB in individuals with negative sputum smear.
Methods: A total of 45 905 sputum samples from 17 850 individuals/subjects were studied over two years (2008: $n = 22 281$ from 8000 subjects; 2009: $n = 23 624$ from 9850 subjects). The samples were first examined for acid-fast bacilli (AFB) by microscopy in four selected TB clinics in Dar es Salaam, Tanzania. Detection by rats was carried out at Sokoine University of Agriculture, Morogoro, Tanzania. The rats systematically screened heat inactivated samples by sniffing and subsequently indicating (signalling) positive samples. Indicated samples were re-examined for AFB by microscopy. Rat's findings were shared with the TB clinics for tracing of detected individuals for further confirmation. The detection of culture confirmed TB in patients with negative sputum smears ($n = 51$) was determined using four rats.
Results: Use of rats for second-line screening increased case detection rate. Of the 8000 subjects analyzed in 2008; 1200 were AFB positive by microscopy (15.4%) while screening by rats yielded additional 344 positive subjects (28.66% increase). In 2009; 1560 subjects were AFB positive (15.8%) out of 9850. The rats detected additional 561 TB positive patients, thus increasing the detection rate by 35.96%. The rats detected 11 out of 51 (21.56 %) of the culture positive smear negative samples.
Conclusion: Trained rats can be a useful tool in second-line TB screening and detection of the difficult smear negative TB cases. Studies continue to standardize the rat's detection and improve the detection of the problematic smear negative TB cases.

PC-101472-15   A comparison of two different size standards for the determination of MIRU-VNTR copy numbers

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Background: DNA fingerprinting of *Mycobacterium tuberculosis* isolates is a powerful tool for studying the molecular epidemiology of tuberculosis (TB). Mycobacterial interspersed repetitive units (MIRU) typing allows high-throughput and discriminatory analysis of *M. tuberculosis* isolates. MIRU-VNTR determines the number of repetitive units at 24 independent loci in the *M. tuberculosis* genome. Precise determination of the size of the PCR fragments is important for calculation of the copy numbers for each locus.

Objective: The aim of this study was to determine if the use of different size standards can result in a variation in reported copy numbers for identical isolates.

Method: Twelve isolates were analyzed by the MIRU-VNTR method as described by Supply et al. using two standards; the MapMarker ROX-1000 (Bioventures) and the GeneScan ROX-1000 (Applied Biosystems) as standards for size determination of the PCR fragments. The PCR fragments were sized and the VNTR alleles were assigned after electrophoresis on a 96-well ABI 377 sequencer with the Gene Mapper (Applied Biosystems) and Peak Scanner (Applied Biosystems).

Results: The two different standards used for size calling reported differences in the size of the PCR fragments for the majority of samples analyzed. For PCR fragments < than 545 bp, the variation ranged between 0–16 bp between the two standards. For fragments > 546 bp, the variation ranged from 2–103 bp. For 18 of the loci analyzed, the difference in size of the PCR fragments resulted in a change in copy number, whereas for the loci MIRU 4 and ETR-A, although a difference in size was observed (from 1 bp [MIRU4] to 59 bp [ETR-A]), the copy numbers remained identical.

Conclusion: Different standards used for size calling can result in discordant MIRU-VNTR results for identical *M. tuberculosis* isolates. For generalisability of MIRU-VNTR data between laboratories, rigorous attention to protocol, standardized reagents and methods for accurate size estimation need to be established.

PC-100201-15   Detection of IP10 in urine is associated with pulmonary tuberculosis and non TB pulmonary disease

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Rationale: Interferon-γ-inducible protein 10 (IP10) is a chemokine involved in the response to *Mycobacterium tuberculosis*. Recent studies have demonstrated that active tuberculosis (TB) is associated with increased IP10 plasma levels suggesting that IP10 detection could represent a marker for TB diagnosis and therapy monitoring. The use of urine would present several advantages when compared to plasma: its collection is non invasive, it does not represent a biological risk for the personnel involved, it does not require special equipment or highly specialized healthcare workers. To date, there are no evidences of the evaluation of IP10 in urine of TB patients.

Objectives: To investigate the presence of IP10 and other chemochines/cytochines in urine of patients with pulmonary TB.

Methods: Urine samples were collected from 59 patients with culture confirmed pulmonary TB before therapy, 30 patients with pulmonary infections other than TB, and 34 healthy donors, all with no signs of urinary tract infection. Levels of IP10, MIP-1α, MIP-1β, IFNγ, TNFα, IL-2, IL-8, RANTES in urine were analysed using a human Cytometric Bead Array Flex SET (Becton Dickinson Biosciences, San Diego, CA) and analysed by flow cytometry (FACS Canto, Becton Dickinson).

Results: The level of urine IP10 was significantly increased in patients with pulmonary (TB and non) disease (median: pg 16.24, IQR:1.29–36.97), when compared to healthy controls (median: pg 0.8, IQR:0–8.4) (*P* < 0.0007). None of the other immune factors analysed was found in urine. A decrease of IP10 levels during treatment was observed in the urine of the 3 TB patients analysed at baseline and after 2 months of therapy.

Conclusions: IP10 is detected in urine of patients with diseases not associated with the genito-urinary system. The presence of IP10 in urine is correlated with pulmonary diseases, and its level decreases after therapy. Further studies are needed to better investigate our findings.

PC-100475-15   Single nucleotide polymorphism in the mammalian cell entry operons of *Mycobacterium tuberculosis*

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Background: Earlier we had reported the differential expression of four mce operons of *Mycobacterium*

tuberculosis; mce1 operon is expressed during exponential phase in broth culture where growth conditions are favorable and mce4 operon is expressed in the stationary phase where bacteria are under stress in a nutritionally depleted environment and also in infected tissues in animals.

Design: We have investigated the extent of polymorphism in all the 16 genes of these mce1 and mce4 operons of *M. tuberculosis* from 112 drug susceptible and drug resistant clinical isolates varying in their drug susceptibility profile and four standard strains (H37Rv, H37Ra, LVS (Low Virulent Strain) and BCG) to discover SNPs using sequenom mass array platform. The data was analyzed to predict the effect of the SNP at the protein level using the available softwares.

Results: We discovered 20 SNPs in the two operons. The comparative analyses of the genes of mce1 and mce4 operons reveal that yrbE1A and mce1A were most polymorphic in mce1 operon and lprN again being most susceptible to SNPs in the mce4 operon. Of 20 single nucleotide polymorphisms (SNPs), 14 were found to be nonsynonymous. 3 of the 14 nonsynonymous SNPs investigated for their pathological relevance to *M. tuberculosis* by PolyPhen and PMut servers were found to be deleterious. It was found that a mutation from proline to serine at position 359 of the native protein of the Mce1A protein was most deleterious. A structural analysis of this mutated protein and the native protein was performed using InsightII.

Conclusion: The analysis revealed that irrespective of drug susceptibility profile of the clinical isolates, mce4 operon is significantly more polymorphic than mce1 operon ($P < 0.0001$). Based on the computational studies work, we predict that the nonsynonymous SNP at mce1A may play a pivotal role in causing functional changes in *M. tuberculosis*.

PC-100534-15   SOCS1 as a regulatory mechanism of proinflammatory IFN-γ-inducible chemokines in pulmonary TB

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Background: T cell IFN-γ is critical for protection against *Mycobacterium tuberculosis* infection and IFNγ-inducible chemokines CXCL9 and CXCL10 which are essential for granuloma formation. IFN-γ can be modulated by Suppressor of Cytokine Signaling (SOCS-1) molecules. IFNγ responses are depressed in patients with tuberculosis (TB) but little is known about the regulatory mechanisms involved.

Methods: We investigated IFN-γ, SOCS-1, CXCL9 and CXCL10 activation in peripheral blood mononuclear cells (PBMCs) of patients with pulmonary tuberculosis (PTB, $n = 23$) with minimal ($n = 2$), mod-

erately advanced ($n = 12$) or far advanced ($n = 9$) disease based on extent of lung parenchymal involvement. Responses were compared with those of healthy endemic controls ($n = 19$). Basal levels of gene expression and responses to *M. tuberculosis* H37Rv sonicate were determined.

Results: In patients with advanced PTB, endogenous levels of SOCS1, CXCL-9, and CXCL10 ($P = 0.02$, 0.05, 0.03, respectively) were raised as compared with moderate disease. Stimulation with *M. tuberculosis* sonicate-induced increased SOCS-1 and CXCL9 and expression in patients ($P : 0.05, 0.02$). Within the PTB group, *M. tuberculosis*-sonicate induced SOCS-1 was greater in moderately advanced as compared with far advanced disease ($P : 0.016$).

Conclusions: Increased endogenous SOCS-1 expression in patients with far advanced disease may lead to down modulation of IFN-γ responses, while decreased *M. tuberculosis*-sonicate induced SOCS-1 expression in far advanced disease may suggest reduced pathogen specific responses in this group. Raised CXCL9 and CXCL10 expression in advanced PTB are reflective of the increased disease associated pathology observed. This study implicates SOCS1 activation as a mechanism for regulation of IFNγ-induced responses in TB patients.

PC-100732-15   Significance of antigen-specific induced TNF-α production for diagnostics and monitoring of TB

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Background: TNF-α is known to be one of the most important factors for protective immunity to TB infection.

Objectives: To determine TNF-α specific immune response of TB patients as a method for differential diagnostics of TB.

Design/methods: Using mixture of secreted TB antigens ESAT-6 and CFP-10, we evaluated the antigen-specific production of TNF-α in whole blood samples obtained from 24 patients with active pulmonary TB (12 adults and 12 adolescents), 12 patients with previous history of successfully treated TB and residual radiographic abnormalities, and 19 patients with non-TB lung diseases (16 patients with pneumonia and 3 patients with lung cancer). TNF-α levels in plasma samples were determined using sandwich ELISA with affinity-purified polyclonal rabbit anti-hTNF-α antibodies raised against full-length human TNF-α as a capture reagent and monoclonal mouse anti-hTNF-α antibody F10 as a detection reagent.

Results: In samples obtained from patients with active TB TNF-α levels induced by stimulation with the mixture of antigens were significantly higher than those in patients with previous history of TB infection—4.92 ± 0.78 ng/ml versus 2.14 ± 0.32 ng/ml for adults ($P = 0.002$) and 3.56 ± 0.8 ng/ml versus 0.96 ± 0.28 ng/ml for adolescents ($P = 0.01$). In one case of extremely severe clinical course of TB, however, induced level of TNF-α was less than 1 ng/ml. In samples obtained from adult patients with non-TB lung diseases induced level of TNF-α was significantly lower—0.96 ± 0.45 ng/ml ($P = 0.02$). In this group only 1 out of 19 patients demonstrated induced level of TNF-α higher than 2 ng/ml.

Conclusion: We concluded that ex vivo induced TNF-α production in response to TB specific antigens may be used for differential diagnosis between TB and other lung diseases as possibly for monitoring immune response against TB infection.

PC-100355-15   TB GIMS: establishing a molecular surveillance system for TB in the USA

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Aims: TB Genotyping Information Management System (TB GIMS) is the first major improvement toward data management of universal TB genotyping since the inception of the National Tuberculosis Genotyping Service (NTGS) in 2004, where state public health laboratories from all TB programs in the United States began voluntary submission of isolates from culture-confirmed patients for molecular characterization.

Intervention and target population: TB GIMS is a secure web-based application for real-time access to routinely collected surveillance information and genotyping results. TB GIMS builds upon the well-established infrastructure of CDC's national TB registry system, the National Tuberculosis Surveillance System (NTSS), and incorporates genotype data to create a centralized database and reporting system of individual patient-level results and TB clusters. For the first time, TB practitioners in the United States have the ability to monitor TB clusters and compare surveillance data and distribution of clusters both locally and nationally.

Results: Reports, tables, and maps show clusters from local and national perspectives and provide patient-level demographic and risk factor results. TB GIMS will alert users about potential TB outbreaks that grow beyond their expected geographic concentration, enabling appropriate allocation of public health resources. This user-friendly design empowers

TB programs to integrate TB genotyping information into routine practice and fosters inter-jurisdictional collaboration about TB transmission helping to interrupt tuberculosis transmission and reduce the impact of tuberculosis in the United States.

Conclusion: TB GIMS is the first TB genotyping tool to combine molecular and patient-level epidemiologic surveillance of *M. tuberculosis*; it will increase the dissemination of epidemiologically relevant genotyping information for public health action.

TB DIAGNOSTICS II

PC-100065-15   Molecular detection of rifampicin and isoniazid resistant *Mycobacterium tuberculosis* isolates

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The emergence and spread of resistant *Mycobacterium tuberculosis* strains poses a serious threat to tuberculosis control. Molecular methods provide rapid detection of resistance to rifampicin and isoniazid comparing to the gold standard proportion method. In our study, the drug susceptibility of 48 clinical *Mycobacterium tuberculosis* isolates detected by proportion method (25 multidrug-resistant strains, 1 strain resistant only to rifampicin, 18 strains resistant to isoniazid and 4 susceptible) is tested using two molecular methods, the Genotype MTBDR plus, Hain Lifescience, Nehren , Germany and MAS-PCR in order to confirm resistance and detect mutation involved. The resistance to rifampicin is detected in 24 cases (22 MDR) using the Genotype MTBDR method and in 25 cases using MAS-PCR (23 MDR). The 531 mutation is found to be the most frequent.

Among the 43 strains resistant to isoniazid, 38 cases were detected using the Genotype method and 39 using MAS-PCR. As expected, the mutation in the codon 531 of *kat*G gene is found to be the most frequent. It is detected in 79% of cases by MTBDR method and in 74.4% by MAS-PCR. The mutation in inhA regulatory region is involved in 20.93% cases using the MAS-PCR and only in 4.65% cases using the MTBDR method. 8 strains are found susceptible to both drugs using the MTBDR method and 7 by MAS-PCR. The correlation between the molecular methods is 96% in detecting rifampicin resistance and 97.44% in detecting isoniazid resistance. Comparing to the gold standard proportion method, the correlation is 90.1% with Genotype method in detecting resistance to rifampicin and isoniazid drugs, and 93.2% with MAS-PCR technique. MAS-PCR

seems to be more sensitive than Genotype MTBDR method, essentially in detecting mutations in the inhA gene. The molecular methods offer a rapid detection of resistant strains and improve management of MDR tuberculosis. Whereas, these methods are less sensitive than the proportion method.

PC-100234-15   Identification of mutations in the alpha subunit of DNA gyrase gene in oflaxacin-resistant *Mycobacterium tuberculosis*

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Identification of mutations in the alpha subunit of DNA gyrase gene in ofloxacin resistant clinical isolates of *Mycobacterium tuberculosis* in Belarus. Fluoroquinolones are being used more frequently for the treatment of multidrug-resistant tuberculosis patients. This study was based on detection of DNA-gyrase gene (gyrA) regions that determine the resistance to fluoroquiolones (quinolone resistance-determining region, QRDRs).Ofloxacin resistance was proved for 22 XDR *M. tuberculosis* strains from 84 clinical isolates by the proportion method. Molecular-genetic analysis of 22 XDR *M. tuberculosis* strains, isolated from TB patients demonstrated their belonging to Principal Genetic Group 1 in 10 cases ($45.5 \pm 10.9\%$), to Group 2 in 8 ($36.4 \pm 10.5\%$) and to Group 3 in 4 ($18.1 \pm 8.4\%$) cases. Mycobacteria of Genetic Group 1 dominate among MDR and XDR-isolates ($P < 0.05$) between 84 isolates. Molecular bases of resistance to Ofloxacin were investigated by determination of mutations in QRDR region of gyrA gene. Frequency of amino-acid and nucleotide substitutions in codons 90 and 94 of gyrA gene of XDR isolates was determined by sequence method. We revealed that mutation in codon 94 (GAC→AAC or GGC, CAC, GTG) was maximal frequent one as it was observed in 12 (57%) of 21 XDR-isolates. Nine (42.7%) of investigated XDR-isolates contained mutations in codon 90 (GCG→GTG) and one isolate had two simultaneous mutations in codons 90 (GCG→GTG) and 94 (GAC→CAC).Polymorphism in codon 95 was identified in all of XDR-isolates but there was no such a mutation in any of Ofloxacin-susceptible isolates. We concluded that determination of nucleotide sequences of fluoroquinolone resistance-determining regions (QRDRs) in the A subunits of DNA gyrase can be used as a molecular test for the detection of Ofloxacin resistance in the bacterium.

PC-100421-15   Differentiation of members of the *Mycobacterium tuberculosis* complex using a Luminex assay

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Background: Rapid differentiation of members of the *Mycobacterium tuberculosis* complex (MTBC) has important clinical and epidemiological applications. Current methods include sequence analysis or probe-based systems such as the Genotype MTBC strip (Hain Lifescience). Sequence analysis can be time consuming, and the GenoType MTBC strips can be cumbersome to work with in large numbers and the data must be manually interpreted from the strip. Molecular differentiation is based largely on single nucleotide polymorphisms (SNPs) within multiple genes in the MTBC genome. The Luminex system allows for simultaneous detection of up to 600 probes for specific nucleotide sequences within a segment of DNA. We have applied this methodology to the identification of the SNPs that are currently used to differentiate MTBC members.
Methods: Primers for PCR and probes for the Luminex assay were developed that corresponded with SNPs in the gyrB, pncA, 16s rRNA genes along with, region of difference (RD) 1. Luminex probes included each previously observed nucleotide at SNP sites. Polymerase chain reaction and hybridization conditions were optimized for each of the PCR products and probes. Probes were coupled to polystyrene beads which were detected using the Luminex FlexMap 3D system. DNA sequences were confirmed using Sanger-based sequencing.
Results: Amplification of the various genes was successful in each of the complex members tested. Probes were hybridized to a panel of strains with sequences representing each of the probe sequences. All of the probes were successfully hybridized and detected using the Luminex system. Optimization of conditions shows that the PCR and hybridization reactions lend themselves to multiplexing of these assays.
Conclusions: The Luminex system is able to provide high throughput, rapid and accurate differentiation of members of the MTBC complex. This system is advantageous due to its rapid turn around time, ability to multiplex, and expandability.

PC-100892-15   Fluoroquinolone exposure and genotypic fluoroquinolone resistance mutations in *M. tuberculosis*

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Background: Fluoroquinolone resistance in *M. tuberculosis* is often associated with mutations at codons 90, 91 or 94 of gyraseA (gyrA), though other mutations are possible. The relationship between duration and timing of fluoroquinolone (FQ) exposure prior to tuberculosis (TB) diagnosis and genotypic fluoroquinolone resistance has not previously been studied.

Methods: All newly diagnosed TB patients reported to the Tennessee Dept. of Health between 2002–2006 who also had TennCare pharmacy benefits were assessed for outpatient FQ exposure in the 12 months prior to TB diagnosis. All *M. tuberculosis* isolates resistant to ofloxacin 2.0 μg/ml by agar proportion underwent sequencing of the entire gyrA gene. Sequencing was performed with an ABI Prism 3730xl DNA Analyzer using Big Dye Chemistry. Applied Biosystem's DNA Sequencing Software was used to collect and analyze raw data. Mutations were identified by comparing study isolates to *M. tuberculosis* H37rV using Polyphred software.

Results: Of the 16 *M. tuberculosis* isolates with phenotypic FQ resistance, outpatient FQ exposure prior to TB diagnosis was documented in 8 (50%). Six of the 8 (75%) resistant isolates with prior FQ exposure had a mutation at codon 90 or 94 (none with 91), compared to only 1 of 8 (12%) without documented outpatient FQ exposure ($P = 0.012$). Resistant isolates with >10 days of FQ exposure or FQ exposure occurring >200 days before TB diagnosis were also more likely to have a mutation at codon 90 or 94 of gyrA than resistant isolates without such FQ exposure (86% vs. 11%; $P = 0.003$ and 80% vs. 27%; $P = 0.05$, respectively).

Conclusion: The common FQ resistance mutations at codons 90 and 94 of gyrA were associated with FQ exposure >10 days in duration and >200 days before TB diagnosis. FQ-resistant *M. tuberculosis* isolates without such exposure were much less likely to have these commonly-described mutations. These findings are important for the development of rapid diagnostic tests for FQ resistance.

PC-101065-15   Evaluation of GenoType® MTBDRsl for rapid detection of resistance to floroquinolone and aminoglycosides

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Aim: Rapid diagnosis of Extensively Drug Resistant TB (XDR) is urgent need to stop outbreaks of XDR. Culture and DST on solid or liquid takes weeks to month to diagnose XDR. GenoType® MTBDRsl a rapid molecular line probe assay (LPA) to detect mutations in the gyrA, and rrs genes for the diagnosis of XDR.

Objective: To address the urgent need for XDR diagnosis and to show the feasibility of implementation of LPA in the developing country.

Methodology: Total 116 proved MDR isolates from MDR treatment program of Nepal were tested for second line drugs, ofloxacin, kanamycin, capreomycin using proportional method on Löwenstein-Jensen. Additionally the GenoType® MTBDRsl assay was performed exactly to the instructions of the manufacturer. All discrepant results were repeated on both methods.

Result: Among the 116 MDR isolates, 80 (68.9%) were susceptible to ofloxacin, kanamycin and capreomycin, 5 (4.3%) were resistant to ofloxacin, kanamycinin and capreomycin (XDR). Resistant to ofloxacin but susceptible to kanamycin and capreomycin were 27 (23.2%), susceptible to ofloxacin and resistant to kanamycin and capreomycin were 4 (3.4%). Out of 32 conventional ofloxacin resistant, 31 (sensitivity 96.9%) were detected by GenoType, of 9 kanamycin and capreomycin resistant, 8 (sensitivity 88.9%). Among the 84 ofloxacin susceptible cases, 84 (specificity 100%) were detected by GenoType, of 107 kanamycin and capreomycin susceptible, 107 (specificity 100%) were detected.

Conclusion: GenoType MTBDRsl assay is a rapid method for detection of ofloxacin, kanamycin, capreomycin resistance with a reasonable sensitivity. In combination with line probe assay detecting resistant to isoniazid and rifampicin, it is a potential tool for diagnosis of XDR-TB within one/two day.

PC-101404-15   The usefulness of real-time PCR for a rapid differentiation of *Mycobacterium tuberculosis*

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Background: Non-tuberculous mycobacteria (NTM) has been increasing in smear positive sputum speci-

mens in Korea. About 8% of smear positive sputum specimens from health centers in Korea turned to be NTM by culture. To prevent mistreatment of patients with NTM, a rapid differentiation is necessary. In this study, we evaluated the usefulness of real-time PCR (RT-PCR) in differentiating mycobacteria in sputum.

Methods: A total of 966 smear positive sputum samples were collected from 25 public health centers in Seoul, Korea in 2009. All samples were mixed with equal volume of 4% NaOH for decontamination. After centrifugation, 2 drops of sediment were inoculated to 2% Ogawa medium. DNA was extracted from sediment using bead beating method and tested by Advansure TB/NTM Real-time PCR kit (LG Life science, Korea).

Results: Of 966 samples, 780 were requested for initial diagnosis and 186 for follow up. 857 (88.7%) were TB positive and 94 (9.7%) were NTM positive in RT-PCR. (Two samples were positive for both TB and NTM.) Compared to culture, sensitivity and specificity of RT-PCR for TB detection were 99.4% and 94.3%. Forty two (5.4%) specimens for diagnosis were negative for AFB culture and 11 (1.4%) were contaminated, but RT-PCR detected TB in 35 and NTM in 9 among them.

Conclusions: RT-PCR was well correlated with culture and showed high sensitivity. However, we found several false results of RT-PCR. Culture failure rate was quite high ($\sim$8%) in diagnostic samples. Therefore, RT-PCR could be useful for differentiating TB from NTM in combination with culture.

PC-101149-15   Assessment of the GenoType® MTBDRsl Line Probe Assay for the rapid diagnosis of XDR-TB in South Africa

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Background: Extremely drug resistant tuberculosis (XDR-TB) is a considerable problem in South Africa and elsewhere. Rapid molecular assays will markedly reduce delays in diagnosis and associated risk of transmission encountered with drug susceptibility testing (DST).

Objective: Evaluation of MTBDRsl® line probe assay [SL-LPA] (Hain Lifescience) for detection of resistance to ofloxacin, amikacin, and ethambutol associated with gyrA, rrs and embB mutations respectively in local isolates.

Methods: SL-LPA assay was performed at a National Health Laboratory Service referral facility, Cape Town, and DST by MGIT 960 at National Tuberculosis Reference Laboratory, Johannesburg on 76 pre-

viously identified XDR isolates also resistant to ethambutol. Ten XDR isolates with mutations in target genes on sequence analysis were also tested by SL-LPA and DST.

Results: Five isolates were contaminated. Concordance between DST findings and SL-LPA on 71 isolates for ofloxacin, amikacin and ethambutol was 100%, 94.4% and 88.7% respectively, indicating that SL-LPA detected resistance to ofloxacin in all 71 isolates while in 4 and 8 isolates respectively, SL-LPA failed to demonstrate resistance to amikacin and ethambutol. Correlation between phenotypic and genotypic findings on the 10 sequenced isolates was 100%.

Conclusion: Results presented here are comparable to those of Hilleman et al. on cultures from a reference laboratory in Germany. The fewer ofloxacin discordant findings may be ascribed to selection of previously confirmed XDR-TB isolates while it is possible that the rrs and embB targets of SL-LPA may not cover all local amikacin- and ethambutol-resistant strains. The SL-LPA shows good promise for rapid diagnosis of XDR-TB.

PC-100202-15   Performance assessment of the GenoType®MTBDRplus test on sputum specimens of suspected TB cases

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Aim: To evaluate the performance of the GenoType® MTBDRplus test for rapid diagnosis of tuberculosis (TB).

Methods: We enrolled 93 TB suspects, in whom 46 had been previously treated with anti-TB drugs (36 were relapse, 6 treatment after failure, 3 treatment after default, one with side-effect) and 47 had not. Sputum specimens were analyzed using GenoType® MTBDRplus test and conventional methods. The GenoType®MTBDRplus test can simultaneously identify TB and determine drug resistance (rifampin (RMP) and/or isoniazid (INH)). Information including results of smears and categories of TB cases were collected.

Results: Of the 93 TB suspects, 90 (96.8%) having culture results, 68 (75.6%) were culture positive for *M. tuberculosis*. Sixty culture positive cases had concordant results, whereas eight cases were indeterminate using GenoType®MTBDRplus test. Nevertheless, of the 14 TB cases identified by the GenoType® MTBDRplus test, 12 were culture negative and two not done. Overall, 74 (79.6%) TB cases were identified using the GenoType®MTBDRplus test, and 17 (23.0%) were resistant to both INH and RMP (MDR-TB), 15 (20.3%) were RMP mono-resistance, seven (9.5%) were INH mono-resistance, 32 (43.2%) were susceptible to both INH and RMP, and three were

indeterminate. Among 19 indeterminate cases, 13 (68.4%) were AFB smear negative. The test was more applicable and accurate for AFB positive specimen. Relapse (83.3%, 30/36), treatment after failure (100%, 6/6), treatment after default (66.7%, 2/3) and new cases with contact history (72.7%, 8/11) were more likely to be identified as TB.

Conclusion: The GenoType®MTBDRplus test is applicable for rapid diagnosis of smear positive re-treatment TB cases.

PC-100164-15 GenoType®MTBDRplus evaluation for rapid detection of MDR-TB isolates in Indonesia

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Background: A challenge in Programmatic Management of Drug Resistant Tuberculosis (DR-TB) is the prompt detection of patients with DR-TB. We validated a rapid detection kit, GenoType®MTBDRplus, for identification of MDR-TB patients in Indonesia.
Methods: We determined the sensitivity and specificity of the GenoType®MTBDRplus assay for detection of isoniazid and rifampicin resistance in 160 *Mycobacterium tuberculosis* isolates with known phenotypic resistance compared with MGIT960 as gold standard.
Results: Of the 160 evaluated strains, 87 (54.4%) strains were concordant in rifampicin resistance and 61 (38.1%) strains were rifampicin sensitive in both tests. In 3 isolates (1.9%) the GenoType®MTBDRplus was false positive and in 9 (5.6%) false negative. For isoniazid resistance 82 (51.3%) strains were resistant and 39 (24.4%) sensitive in both tests, while in 3 (1.9%) strains the GenoType®MTBDRplus was false positive and in 36 (22.5%) false negative. Sixty-three strains (39.4%) were designated as MDR by both tests and for 63 there was agreement for non MDR. Three strains (1.98%) were false positive and 31 (19.4%) strains false negative by GenoType®MTBDRplus. The sensitivity of the GenoType®MTBDRplus for detecting rifampicin resistance, isoniazid resistance and MDR was 90.6% (95% confidence interval [CI] 82.5–95.4), 69.5% (95%CI 60.2–77.5) and 67.0% (95%CI 56.5–76.2), respectively. The specificity of GenoType®MTBDRplus compared to MGIT960 for detecting rifampicin resistance, isoniazid resistance and MDR was 95.3% (95%CI 86.0–98.8), 92.9 (79.4–98.1), and 95.5% (86.4–98.8) respectively.
Conclusion: Although sensitivity and specificity of the of GenoType®MTBDRplus in detecting rifampicin, isoniazid and MDR resistance was lower than

what is reported in the literature the GenoType® MTBDRplus can be useful for screening for MDR-TB in Indonesia.

PC-100489-15 Evaluation of colorimetric methods for detection of pyrazinamide resistance in *M. tuberculosis*

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Aim: The direct detection of pyrazinamide (PZA) resistance in *Mycobacterium tuberculosis* is sufficiently difficult so that many labs don't attempt it. Most PZA resistance is caused by mutations that inactivate the pyrazinamidase enzyme needed to convert the prodrug PZA to its active form. The purpose of this research was to evaluate two newer and simpler methods—the nitrate reductase (NRA) and malachite green microtube (MGMT) assays—using nicotinamide (NIC), for detecting resistance to PZA.
Methods: The PZA susceptibility was assessed in 102 *M. tuberculosis* strains by the NRA and MGMT assays and the results were compared with those obtained by the classic Wayne assay. Mutations in the pncA gene were identified by sequencing the pncA gene from all isolates in which PZA-resistance was detected by any of the three methods.
Results: The NRA and MGMT assays showed sensitivities of 93.75% and specificities of 97.67%. The agreement between both methods and the Wayne assay was 97.05%. Mutations in the pncA gene were found in 14 of 16 strains that were PZA resistant, and in 1 of 4 strains that were sensitive by the Wayne assay.
Conclusion: The NRA and MGMT assays employing NIC are simple, accurate, inexpensive and robust alternatives for the rapid detection of PZA resistance in limited-resource countries.

TB INFECTION CONTROL

PC-100092-15   Implementation of tuberculosis infection control strategy in Zambia

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Background: Introduction of tuberculosis infection control in Zambia has provided an opportunity to address the country's efforts to combat TB infection. This presentation describes the process and challenges, associated with the roll out of TB infection control in Zambia.

Methods: In 2007, Zambia developed a national TB infection control strategy that included development of national guidelines, training key staff in implementation of infection control measures and facility risk assessment visits to two reference laboratories and three hospitals.

Results: 77 doctors, nurses, clinical officers, environmental and laboratory specialists and building professionals from all nine provinces were trained in the national TB infection control guidelines. Including the building professionals and environmental specialist ensured appropriate renovations in the TB clinics and laboratories. The facility risk assessments visits found the need for administrative and environment control measures including patient triage and cough etiquette in all out-patient units including ART clinics. Maximum utilization of natural and mechanical ventilation in medical wards and laboratories was also assessed. Two of the three hospitals evaluated for possible programmatic management of multidrug-resistant TB were recommended as favourable sites.

Conclusion: Zambia can use the momentum of the national TB infection control scale up strategy to facilitate implementation of measures countrywide. Reducing risk of TB transmission in HIV care and treatment sites remains a challenge that will require implementation of strategies in collaboration with key partners. The existing efforts in general infection prevention and control committees at all levels of health care provide an entry point to emphasize implementation of TB infection control, including TB screening of health care workers.

PC-100463-15   Using wind-driven roof turbines to improve TB infection control in primary care clinics, Khayelitsha

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Background: Nosocomial TB transmission may contribute substantially to the TB burden in many settings, particularly those with high HIV. Despite this, TB infection control in health facilities is often neglected. Although natural ventilation is now recognised as an important strategy for reducing transmission, there is a lack of data on effective interventions in the real world. We aimed to assess the effectiveness of wind-driven roof turbines (Figure) to increase ventilation in clinic rooms in Khayelitsha.

Figure   Wind-driven roof turbine.

Method: Air changes per hour (ACH) were measured using a carbon dioxide gas technique, where gas is released into a room, mixed and equilibrated, and concentration-decay assessed over time. 3 scenarios were compared; a) doors and windows closed, b) only window open and c) only installed roof turbine and either wall or door grate open. Wind speed was measured simultaneously, and ACH data analysed by wind speed category.

Results: To date, measurements ($n = 116$) have been conducted in 4 rooms in 3 different primary care clinics. These rooms represent different building and roof designs currently used in Khayelitsha. At average wind speeds less than 10 km/hr ($\sim$5 knots), mean ACH was 1.9 (range 0.1–3.5, $n = 45$) for doors and windows closed, 5.3 (range 2.0–10.6, $n = 23$) for an open window and 9.8 (range 6.7–13.3, $n = 18$) for the turbine and air-inflow grate. These differences were consistent in each of the 4 rooms. ACH increased at wind speeds >10 km/hr.

Conclusions: Preliminary results suggest that wind-driven roof turbines have the potential to improve ventilation in health care settings. At relatively low wind speeds, mean ACH are close to 10; a level recommended as reducing the risk of TB transmission.

Roof turbines are low-cost, low-maintenance and less dependent on human behaviour since they are effectively unable to be closed in cold weather. Wind-driven roof turbines appear to offer important opportunities for infection control and reduction in transmission risk.

PC-100759-15   Tuberculosis infection control risk assessment score to predict TB in healthcare workers

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Background: TB infection control measures should prevent nosocomial transmission of *Mycobacterium tuberculosis* in healthcare facilities. To measure the risk of *M. tuberculosis* transmission in facilities, a TB infection control risk assessment tool was developed by the Centres for Disease Control. This study aimed to determine whether a TB risk assessment tool can identify high risk clinics (defined as clinics with at least one case of TB disease in healthcare workers) in countries with a high incidence of TB.
Methodology: During 2009 132 primary healthcare facilities were evaluated with a risk assessment tool for TB infection control and TB cases in health care workers in five provinces in South Africa. An equal score was assigned to each area of risk. The mean score was chosen as a cut-off point to define high risk and low risk facilities for *M. tuberculosis* transmission.
Results: 87 facilities were classified as high risk and 33 as low risk (missing data in 12 facilities). 26 (30%) high risk facilities and 18 (55%) low risk facilities had healthcare workers with TB ($P = 0.007595$). The risk ratio was 0.5479 (CI 0.3501, 0.8574) for a high risk facility to have TB cases. There was an inverse relationship between the risk score and the presence of TB cases.
Discussion: Further analysis will include stratification according to TB incidence at facility level. It is essential to determine whether a risk assessment tool can be used in high incidence areas to identify clinics where nosocomial transmission of *M. tuberculosis* occurs.

PC-100497-15   Implementation of intensive infectious control measures in Shaktersk TB dispensary, Ukraine

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Setting: After trainings on infection control (IC) carried out in Donetsk oblast with the participation of WHO and with the financial support of local charitable Foundation 'Development of Ukraine', the decision was made to implement intensive IC measures in Shaktersk TB dispensary.
Aim: To decrease TB morbidity among medical and non-medical staff and to reduce acquired resistance of Micobacteria tuberculosis (MBT) to anti-TB drugs.
Methods: Plan of implementation of IC measures and tools was elaborated, the following measures were introduced:
   —high risk zones were defined;
   —flows of patients according to their sputum smear status were separated;
   —observation wards for patients with unknown smear status were selected;
   —patients were settled to the wards according to their sputum smear status;
   —patients and medical staff are provided with masks and respirators;
   —patients receive meals in their wards;
   —every ward for smear positive patients is equipped with UV-lamp;
   —algorithm of patients' transference to other specialists for consultations is developed.
Results: TB morbidity among the staff of TB dispensary for the last 4 years (2006–2009) has decreased from 13.3 (2 patients) to 0 per 1000. Besides acquired drug resistance among patients of TB dispensary also has trend to decrease from 10.6% (7 patients from 66) in 2008 to 3% (2 patients from 67) in 2009.
Conclusions: Introduction of all kinds of IC measures and tools (administrative, environmental and individual respiratory protection) allowed decreasing acquired drug resistance among patients and risk to get TB among medical and non-medical staff.

PC-100446-15   Impact of TB infection control interventions in Cacadu District, Eastern Cape Province, South Africa

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Aim: To address gaps in and evaluate the impact of interventions in infection control in Cacadu District.
Methods: A series of once-off infection control interventions were conducted in collaboration with CSIR and provincial and district health departments. The training focused on district, sub-district and health facility managers and professional as well as lay staff. An environmental officer was trained to do infection control assessment and support the district. Mechanisms for separating TB suspects were prioritised, non-clinical workers (cleaners) were trained as 'cough

officers', and cough etiquette posters were developed and displayed in facilities. Pre- and post-intervention data were collected at 34 health facilities (primary health care clinics, community health centres and hospitals) to gauge the impact of the interventions. The baseline and first follow-up wave of quantitative data have been collected and analysed.

Results: Improvements in infection control were noted after the completion of the intervention as additional facilities implemented the following practices/policies: an infection control coordinator ($n = 1$); collect sputum in front of a window or outside ($n = 2$); immediately refer patients coughing more than two weeks for sputum testing ($n = 3$); an open window policy ($n = 3$); health education on infection control ($n = 4$); home-based carers/clerks who actively seek out possible TB suspects ($n = 5$); an infection control policy ($n = 5$); separation of patients with a cough from other patients ($n = 6$); and a designated person responsible for opening windows ($n = 7$).

Conclusion: TB-related infection control awareness and pro-active attempts at infection control have markedly improved. Although a once-off training effort resulted in significant improvement in infection control, gaps remain and need to be addressed and monitored in follow-up training and assessments.

PC-100637-15 Contextual influences on nursing prevention and control of *Mycobacterium tuberculosis* in a South African setting

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Background: We investigated nurses' perspectives on tuberculosis (TB) infection prevention and control (IPC) practices to identify factors associated with nosocomial transmission.

Design/methods: Qualitative design using semi-structured interviews with a purposive sample of 20 nurses in a large tertiary hospital, Cape Town, South Africa where the TB notification rate is >1000/ 100 000. Data were analyzed using a thematic approach.

Results: Interconnected themes included: delayed patient presentation to hospital; concerns and stigma around TB; adherence to IPC measures; training and education; communication; work load; and the sense of duty to provide care. Nurses expressed concerns about infection risk to both staff and patients. Patients were perceived to present late; patient communication with health staff was limited by cultural differences and language problems. IPC practices were regarded as weak and inconsistent and wards lacked isolation facilities and personal protective equipment, particularly those not routinely dealing with TB. There

was a perceived lack of TB training for nurses, and limited education for patients. Nurses had mixed views regarding the role of traditional healers in TB treatment support to improve timely patient presentation to hospital.

Conclusions: IPC practices, training of nurses and patient education are perceived by nurses to be suboptimal in this large hospital and may be associated with increased risk of nosocomial transmission. The provision and appropriate use of IPC measures must be improved across all wards. Concerns and stigma around TB among both healthcare providers and patients should be addressed. Contextually appropriate training of nurses should be a priority in high TB-burden hospitals.

PC-100880-15 Collaborative tuberculosis infection control pilot project in Mexico

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Background: TB infection control (TBIC) is important for TB prevention. In TB-endemic countries, TBIC programs are limited. The purpose of this project is two-fold: to use training at the institutional level to form the basis of state and national plans for TBIC and to build capacity in TBIC at all levels. A major challenge has been that in order to be flexible to the needs of the National TB Program (NTP), work plans were modified once work was underway. Also, the large number of partners involved presented logistic and communication challenges.

Intervention: In August 2009, we launched a pilot TBIC training project in Mexico. Three states with varying TB burdens were chosen. One hospital and one primary health center were identified in each state. The pilot consisted of TBIC assessments followed by a three day interactive course finalized by the development of a TBIC plan tailored to the participants' individual work setting. During the course participants reviewed institutional air flow and reviewed where healthcare workers (HCW) and non-infected patients come in contact with infectious TB patients.

Results/lessons learned: As of March 2010 two courses were conducted with 85 participants, representing two hospitals, three clinics, one lab and TB program staff. Four institutional plans have been developed and two state TBIC plans are being developed. The main lesson learned is that the demonstration of

risk of TB to HCW and non-infected patients leads to rapid, inexpensive changes in practice and to institutional commitment to the concepts of TBIC. This practical lesson is forming the basis of the development of a National Plan for TBIC.

Conclusions/recommendations: The development of strategic TBIC plans is as ambitious as it is important. Evaluation of this project will require realistic indicators that are relevant to the institutions involved and the NTP. Governmental support will be necessary for broad scale implementation.

PC-100888-15   TB infection control in the era of expanding HIV treatment: lessons learnt from South Africa

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Background: Delays in TB diagnosis and treatment initiation, especially with overcrowding and poor ventilation, facilitate nosocomial transmission of TB among patients and healthcare workers (HCWs). As HIV programs in resource-limited settings provide more TB services, the need to implement TB infection control (TBIC) measures is increasingly important. We describe lessons learnt from implementing TBIC in the Eastern Cape Province, South Africa.

Intervention: An innovative model of TBIC was implemented at HIV care and treatment facilities, focusing on HCW motivation to protect themselves through activities that promote rapid identification of individuals with TB and prompt initiation of TB treatment. Based on the findings from baseline risk assessments, TBIC committees were established and TBIC plans developed, which included: staff training; cough screening, triage and separation of patients with suspected TB; education and supplies to promote cough hygiene; rapid TB diagnosis and treatment initiation; improved natural ventilation; and staff protection. Monitoring and evaluation methods included implementation of a triage register, with monitoring of time spent in the facility of patients with and without chronic cough.

Results: TBIC programs were implemented in 28 facilities, with TBIC committees established and plans developed in 20 of these. With triage, time to consultation at a model program averaged 15 min for TB suspects, compared to 146 min for non-suspects ($P = 0.001$), and total time at the facility averaged 44 minutes for TB suspects, and 174 minutes for non-suspects ($P = 0.003$). Challenges remaining include full separation of patients with suspected TB from other patients and reluctance of patients to accept fast-tracking.

Conclusions: Effective triage systems can be implemented in HIV care and treatment facilities using a systematic approach, focusing on motivating HCWs to protect themselves by reducing source infectiousness.

PC-101440-15   TB infection control in Afghanistan: the state of affairs

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Background: In Afghanistan, one of the WHO designated high burden countries for Tuberculosis (TB), TB incidence rates continue to climb. In order to better understand the current situation, identify gaps and introduce the newly developed TBIC standard operating procedures, an assessment of TB infection control (TBIC) practices in health facilities was conducted.

Methods: A team from TBCAP (Tuberculosis Control Assistance Program) and the National Tuberculosis Program (NTP) visited Herat and Kabul Provinces. A total of 12 health facilities, ranging from basic and comprehensive health centers, district and provincial hospitals to specialized TB hospitals, were assessed using a standardized tool. The assessment team conducted a formal evaluation of each facility, documenting administrative, environmental and personal protective controls through observation, review of charts and supplies, the taking of environmental measurements such as air flow, room size, etc as well as interviewing key staff about existing conditions and practices in their facilities. Following the assessment, the NTP/TBCAP team introduced the newly developed TBIC Standard Operating Procedures, trained the staff and disseminated IEC materials.

Results: Facilities with a designated IC Officer were found to have improved IC practices compared to those without. Some of the gaps identified were; staff, in general, were poorly trained, patient flow patterns overall were counter to TBIC, less than 30% of patients were being referred to well ventilated areas for sputum collection and less than 25% of facilities had operating ceiling, wall or exhaust fans.

Conclusion: Not surprisingly, the overall level of TB IC being practiced at the health facilities was minimal. Many simple, low cost, easily implementable interventions were identified for improving TBIC. An adjusted work plan was developed incorporating the findings and recommendations of the team and is currently being implemented.

PC-100492-15   Intensive on-job training for district supervisors improves overall TB infection control activities

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Background: With funding from USAID, the TB Control Assistance Program (TB CAP) supported twelve districts to implement TB Infection Control (TB IC) activities. After 12 months, very little progress was seen in the implementation of TB IC activities at facility level, except for Manafwa district. Health workers from Manafwa district and The Union/TB CAP staff were engaged to provide onsite support to district supervisors in three poorly performing districts; an assessment was done after seven months to monitor progress.

Objective: To provide intensive on-job support to district supervisors and assess level of implementation of TB IC activities before and after this support.

Methods: Eleven facilities were purposefully selected from Mbale, Soroti and Bukedea districts, which were closest to Manafwa. At the district, 2 technical staff from Manafwa plus a TB CAP staff member were joined by the District TB/Leprosy Supervisor (DTLS) and the District HIV Focal Person (DHFP). At the health facility, an assessement of level of implementation of TB IC activities was done using a standard semi-strucured questionnaire and an observation checklist. Gaps were identified and on-the-job training done for district supervisors and health workers. After 7 months, an assessment on TB IC was done for 14 facilities; 8/11 and 6 additional supported by district supervisors.

Findings: See Table.

Table   Proportion of facilities that achieved the TB IC parameters

TB IC Parameter	Initial assessment (n = 11) %	Assessment after 7 months (n = 14) %
Health worker trained in IC	82	93
Designated TB IC Officer	0	100
Risk assessment done	64	100
TB IC plan developed	27	100
Sputum collection area available	0	93
Triage system in place	18	100
Well ventilated out-patient department*	0	64
Health education TB IC	18	93

*Windows were not routinely opened.

Conclusion: Class room training of health workers needs to be reinforced with intensive on-job training for district supervisors to improve implementation of TB IC activities at facility level.

PC-100401-15   TB infection control implementation and training in Donetsk oblast, Ukraine

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Background: Since 2006, WHO has been assisting implementation of MDR-TB Project in Donetsk oblast with financial support of the Charitable Foundation 'Development for Ukraine'. One of activities is to support infection control (IC) in Donetsk oblast by training staff on TB IC and procurement of equipment for MDR-TB wards. Relevance of TB IC resulted from high rate of new multidrug-resistant TB (MDR-TB) cases of 17.9%, and incidence in TB facilities staff (from 8 to 23 cases annually). Aim is to prevent TB transmission in TB facilities.

Methods: 4 specialized MDR-TB wards for 200 beds were opened in Donetsk oblast. TB IC assessment mission, two-day IC workshop and follow-up IC training was organized in 2009 with participation of representatives of FILHA, CDC and Russian experts. To support implementation of IC measures, WHO purchased and distributed IC equipment (UV-lamps, respirators) for 4 TB facilities of Donetsk oblast. IC working group was established in oblast consisting of TB and epidemiology specialists, WHO and charitable organizations members.

Results: 4 MDR-TB wards were equipped with exhaust and supply ventilation. Administrative, respiratory and partially engineering controls (bactericidal irradiators) are implemented in the rest of facilities. 50 specialists from Donetsk oblast (including penitentiary system) and central level representatives were trained. IC implementation progress is monitored. 7 facilities have IC plans developed. Recommendations on provision of respirators for medical workers regarding risk zones are being prepared.

Conclusions: Difficulties in IC implementation: lack of normative base, insufficient training, shortages in financing the procurement of exhaust and supply ventilation, lack of measuring tools to assess IC efficiency. In order to introduce quality IC measures IC protocol should be developed and approved on country level, trainings to be continued and IC guidelines to be developed.

TB PROGRAMME CASE DETECTION

PC-100792-15   Public private mix in TB control, NWFP, Pakistan

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Aim: To improve case detection rate in the province through the involvement of general practitioners. To go beyond the 70% case detection rate and universal DOTS with 100% coverage, the involvement of the private sector through PPM initiative is mandatory.
Methods: TB Control NWFP and GTZ in collaboration with Pakistan Chest Society developed operational guidelines to facilitate the involvement of general practitioners in TB DOTS. The general practitioners assist TB Control Programme NWFP in delivery of TB care to a defined area of population. They follow NTP protocols for diagnosis and management of TB suspects and TB cases. The GPs send their patients to public sector diagnostic centres or to designated private laboratories The following stepwise approach was developed to implement the project: 1) Orientation seminars for general practitioners, 2) Signing of Memorandum of Understanding with GPs, 3) Training of GPs, 4) Supply of stationery and drugs to clinics, 5) Training of laboratory technicians, 6) Training of clinic support staff, 7) Field support visits, 8) Data collection from clinics on quarterly basis.
Results: PTP-GTZ model has registered 1254 patients (all forms) in 2008. Of them 422 were new sputum smear positive representing 34% of total. The total number of cases registered in 2008 represented 4% of all registered TB cases (31108) in NWFP during the said year. The treatment outcome for the year 2008 was encouraging: the treatment success rate stood at 93%, with the default rate being 2.0% only. This compares with a treatment success rate of 94% and a default rate of 2.0% for 2008 for all analysed cases of NWFP.

	Patients registered in PPM Project (January 2008 to 31st December 2008)				
	1st Qtr 2008 NSS+/All	2nd Qtr 2008 NSS+/All	3rd Qtr 2008 NSS+/All	4th Qtr 2008 NSS+/All	All Qtrs 2008 NSS+/All
Peshawar	63/177	55/183	36/133	41/133	195/626
Mardan	35/126	40/122	43/109	28/70	146/427
Nowshera	4/27	5/41	19/42	32/69	60/179
Charsadda	0/0	0/0	11/11	10/11	21/22
04 Districts	102/330	100/346	109/295	111/283	422/1254

Conclusion: Only 30 GPs were involved in this model. They have contributed 34% new SS+ cases in 2008. Increasing the number of GPs and the expansion of this model to other districts will further increase the case detection rate and the geographic access of TB DOTS to the general population.

PC-100106-15   Community tuberculosis care initiatives in resource-limited rural settings

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Introduction: Before 1997, Community tuberculosis (TB) care was virtually non-existent in many communities in sub-Saharan Africa and in Kenya in particular. Since 2008 when the community strategy policy was implemented in Nyandarua south District, Kenya, a greater impact has been evident.
Nyandarua South District Profile
- District population—396 278
- 40% live below the poverty line
- HIV prevalence is 6%
- 2 Hospitals
- 2 health centers
- 13 TB sites
- 5 ART sites

Objectives: The objectives of community TB care are to contribute to intensified case detention rate from 50% to 70% and to contribute to treatment success rate from the current 84% to 87% by 2010.
Methods:
- Analysis of households was conducted and mapping done in the whole district; 1000 households comprise 1 (one) community unit, 80 community units in all; 50 community health workers (CHWs) per unit.
- Community health workers trained, engaged and supervised.

Results:
- Increase in case finding from 34 in the 4th quarter 2007 to 103 in 4th quarter 2009.
- Reduction in new smear positive default rate from 5% in the 1st quarter 2008 cohort to 0% in the 4th quarter 2008.
- Scale up of CHW—referred cases from 0% in 1st quarter 2008 to 6% in the 4th quarter 2008 cohort.
- Increased awareness on tuberculosis issues; new smear positive last smear not done reduced from 5% in the 1st quarter 2008 to 2% in the 4th quarter 2008.

Conclusion: Community based TB care is a feasible, acceptable and cost-effective way to deliver TB DOTS services.

PC-101308-15   Social mobilisation: a means to increase TB case finding

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Introduction: The ZAMBART project has taken part in the Zambia and South African TB and AIDS Reduction (ZAMSTAR) study. One of the interventions, enhanced case finding (ECF) was aimed to reduce the burden of TB in communities through social mobilization. This poster covers 8 Zambian communities where ECF was implemented from August 2006 until September 2009.
Objective: Evaluate the proportion of TB-suspects whose sputum was examined due to ECF.
Method: Social-mobilization activities were used to disseminate messages in the communities on TB, HIV and stigma. Key messages disseminated information regarding TB-transmission, -diagnosis and -treatment. Sputum samples were obtained, transported and examined at the clinic lab. Participants with positive smears were traced and referred for TB-treatment.
Results: Overall 14 797 individuals accessed sputum smear examination through ECF meaning 34% of individuals whose sputum was examined at the clinic came through ECF. 1081 individuals (7.3% of all participants) were found to be smear-positive, minimally 915 participants (85%) were put on treatment. Additionally 149 smear negative participants ended up on treatment, due to referral to standard clinical care. In comparison with the TB-notifications ECF contributed 9.0% of the total notifications of new patients, and 27% of the total number of registered new smear positive notifications.
Conclusion: ECF substantially increases the number of sputum samples examined at the clinic and leads to an increased number of new TB-cases and/or earlier diagnosis of TB. Our findings support the belief that ECF may have an important role in reducing the burden of TB in communities.

PC-100699-15   Contact investigation experience: tertiary government hospital in Metro Manila, Philippines

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Background: The Lung Center of the Philippines, a government owned, corporate tertiary hospital, is the first public health facility engaged in implementing the Programmatic Management on drug resistant TB in 2005. LCP is one of the 5 Manila treatment centers implementing the GLC-approved PMDT management. Since 2003, contact investigation as one of the important activities in Programmatic Management for drug resistant TB started in 5 treatment centers under Global Fund. All household members residing with index case for a period of 3 months are included in contact investigation. Investigating individual contacts of infectious TB cases is time consuming procedure that conducted routinely in countries with high-resources and low TB prevalence. National TB programmes of low or middle-income countries have not yet established clear approaches to perform such activities, even in countries with high MDR prevalence. Data from a wide range of countries have shown that the prevalence of active TB is high among contacts, particularly among household members (up to 5%).
Methods: Comprehensive interview, physical examination were done to all household contacts of drug resistant TB. Laboratory procedures like chest X-ray exam was done and once it showed findings of infiltrates, sputum examination and culture were requested. Tuberculin testing is done to all children less than 5 year old even without symptoms. Screening household contacts are free of charge.
Results: Partial data on contact investigation from LCP treatment center showed 1013 contacts were identified in 234 index cases confirmed drug resistant TB, 771 (76%) household contacts were traced; 142 (18.4%) had findings on chest X-ray; submitted for AFB examination and TB culture. Five (3.5%) smear positive cases are placed on treatment.
Conclusion: Initial findings signify importance of contact investigation in high prevalent countries. Policies and guidelines are highly recommended.

PC-100964-15   Assessment of TB detection in three regions of the Russian Federation

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Background: TB diagnostic delay, including TB patient, health system and total delays, affects effectiveness of TB control.
Method: Data from national recording and TB01 forms for 690 new pulmonary TB cases notified during 2 quarter 2009 in 3 Russian regions were evaluated, and 480 out of them were interviewed. Delays longer than the median values were used for measure of association with different factors.
Results: The median patient delay made 20 days (Q25:8; Q75: 61). The median health system delay from the first visit to any health provider (HP) to diagnosis was 21 days. The total delay was 49 days (28;

95). Incomplete secondary education was strongly associated with late first visit to HP (OR = 3.0 [CI 95% 1.4; 6.9]). Cough among the first symptoms was also associated with late referral to HP (OR = 0.5 [0.5; 0.9]), while the chest pain made patients earlier to visit HP (OR = 2.9 [1.2; 6.9]). No association was found with employment, and with status in a family as a provider. There was difference between patients from rural and urban areas. Predictive for patient delay there was belonging to socially non-engaged group of population, while socially active patients earlier presented to health providers. Meanwhile those delayed with the first visit to HP had more chance to have ss+ and cavitary TB (cv+). There was no difference due to concomitant diseases, alcohol abuse and age. For the system delay age and gender did not matter, while socially engaged patients after presentation to HP had longer period until TB diagnosis against non-engaged (OR = 0.7 [0.5; 0.96]). Ss+ and cv+ allowed quicker diagnosis. For the system delay the first reference point mattered—the longest delay associated with reference to PHC settings, the shorter system delay associated with reference to district and regional TB dispensaries.

Conclusion: Patients and health system equally contribute to delay in TB diagnosis in Russia and need focused efforts to improve TB case-finding.

PC-101548-15   Determination of TB treatment delay in southern Nigeria

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Introduction: Tuberculosis is a highly infectious disease. Early diagnosis and prompt treatment of TB cases is an important strategy in TB prevention and control. Thus, passive case identification of TB suspects, sputum examination for diagnosis and prompt treatment using DOTS strategy are key elements in the national guideline for TB control programme.

Objective: The aim of the study is to determine the time interval between diagnosis of smear-positive TB cases and commencement of treatment in DOTS facilities in southern Nigeria.

Methodology: The study was carried out in 20 health care facilities involved in TB management in southern Nigeria. The facilities studied included tertiary, secondary and primary health care facilities from public and private sectors. Data were collected through review of records of registered patients July–September 2009. Data on socio-demographic characteristics, sputum smear result, date of diagnosis and date of commencement of treatment were extracted and analysed using SPSS 15.0 software.

Result: A total of 269 smear positive TB cases were

studied. One hundred (38%) of them commenced treatment within 3 days of smear examination for diagnosis, while 59 (22%) commenced treatment between 4–7 days of diagnosis. Eighty one patients (30%) were started on anti-TB treatment between 7–30 days of diagnosis, while the remainder (10%) commenced after 30 days (1 month). Ten percent the facilities surveyed still observed obsolete practice of compulsory admission of patients during the intensive phase of treatment.

Conclusion: The study revealed that forty per cent of sputum smear positive TB cases in southern Nigeria do not receive anti-TB treatment until after one week of diagnosis. The study underlines the need to further explore factors responsible for delay in commencement of TB treatment following diagnosis in Southern Nigeria.

PC-100308-15   Estimate of the contribution of the private sector in TB case notification in Pakistan

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Background: Many studies show that a substantial number of TB cases are managed in the private sector in Pakistan. NTP Pakistan started various PPM ventures in 2004 and since then the number of cases treated by the private sector is increasing.

Objective: To estimate the contribution of various types of private providers in TB case notification in Pakistan in 2009 and analyze the trends in cases notification from the private sector since the implementation of PPM.

Methodology: This was a cross sectional study. Like other HBCs disaggregated is not routinely collected from the private sector in Pakistan. For the purpose of this study, TB cases data was collected from various private providers. The data was also analyzed on basis of various PPM models implemented in the country.

Results: The contribution of the private sector increased significantly from 2004 to 2009. During 2009, PPM contributed to 16.1% cases in the national data, compared to 0.1% in 2004. A fluctuating trend was observed in the PPM contribution, which

	Total cases registered in 2008	Treatment success in 2008	Contribution (%) in National Data in 2008	Total cases registered in 2009	Contribution (%) in National Data in 2009
	Private Sector contribution in TB Control				
District led model	1458	94%	1%	2862	1.1%
Franchise model	12065	88%	5%	6254	2.3%
NGO led model	10096	90%	4%	19582	7.3%
Solo hospital	9545	71%	4%	14464	5.4%
Total Contribution in National Data	33164	84%	13%	43162	16.1%
	251495			267451	

mainly indicate relationship with the funding for PPM. Among the four PPM models, NGO led model yielded maximum number of cases (7.3%), followed by solo hospital model (5.4%), franchise model (2.3%) and district lad model (1.1%).

Conclusion: PPM has a definite contribution in the national data and there is a need to assess the efficacy and cost effectiveness of various implementation models. Sustainability is a major issue in PPM and must be addressed at the proposal development stage.

PC-101376-15   TB control in hard-to-reach area through special interventions

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Introduction: BRAC, an NGO in Bangladesh, providing TB services in collaboration with NTP. BRAC undertook special project under FIDELIS funding to enhance new smear positive case detection. The project also included 17 sub districts of hilly and hard to reach an area which is a residence of many indigenous groups of people covering 1.19 million population. The case detection rate of this area was comparatively lower than the average BRAC supported area of Bangladesh.

Objective: To increase case finding and sustain cure rate with in a hard to reach area.

Interventions: Besides routine TB services, some special interventions were taken under the project from October 2008 to December 2009 especially to reach the indigenous population. The intervention was orientation of traditional leaders. Additional outreach sputum collection centers in hard to reach areas with incentive for volunteers were launched. Posters and leaflets on TB messages were printed in indigenous languages and were distributed. Other activities included miking, school quiz, drum beating in community & market places.

Results: From October 2008 to December 2009 total case was 1223 and smear positive cases was 1069. Among the total cases 53% were indigenous people. By December 2009, new smear positive case detection increased to 72 per 100 000 which were 58 per 100 000 before the interventions. Treatment success rate of NSP patients up to June 2009 was more than 90%.

Conclusion: Special interventions are needed to strengthen tuberculosis control for hard to reach area and to reach special group of population and it needs to be sustained.

PC-100416-15   How many tuberculosis suspects do not complete diagnosis?

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Background: The time and cost burden of tuberculosis (TB) diagnosis is thought to cause many TB suspects to drop out of the diagnostic process. Default during diagnosis is not routinely monitored and the magnitude of this problem has not been evaluated on a large scale. This study quantifies default during diagnosis across all diagnostic centres in 9 districts of Pakistan.

Methods: Data on suspects attending 127 DOTS-reporting diagnostic centres over the period July–September 2008 was collected and analysed. If a suspect submitted a first specimen but did not return to submit a second specimen, this was categorised as default during diagnosis. If a suspect defaulted after submitting one specimen, and that specimen contained acid-fast bacilli, the suspect was categorised as a smear-positive defaulter. Point estimates of the proportion of suspects defaulting during diagnosis, and the proportion of smear-positive cases defaulting during diagnosis were calculated.

Results: Data was collected on 12 216 TB suspects across 120 diagnostic centres. Of these, 1573 TB suspects (12.9%, 95% CI = 12.3–13.5) defaulted during diagnosis. There was considerable inter-district variation in rates of default during diagnosis; districts with over 500 suspects registered per quarter had higher default rates than districts with fewer suspects ($P < 0.000$). A total of 2058 smear-positive cases were detected, of which 107 (5.2%, 95% CI = 4.2–6.2) defaulted during diagnosis and could not be started on treatment. Male suspects defaulted slightly more frequently than female suspects ($P = 0.0268$).

Conclusion: Default during diagnosis is a frequent occurrence causing smear-positive cases to remain untreated within the community. Strategies to reduce default during diagnosis need to be implemented, especially in districts with high suspect burdens.

PC-101116-15   Tuberculosis case finding and its determinants in the Eastern Mediterranean Region

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Background: A hypothetical model has been developed to evaluate the efficiency of the case finding process in 22 countries of the Eastern Mediterranean Region. The model is based on the patient's pathway to care in a stepwise approach from the community

to the TB management units and addresses all the components of the Stop TB strategy.

Design/methods: Process and outcome indicators were used to measure the national tuberculosis control programme performance at each level of the model. Various data sources were used to collect the necessary information retrospectively to measure these indicators. A scoring system was applied to measure performance using these indicators, from 0 to 4, with the higher score reflecting better performance, and '0' if information is not done or not available. The association between performance—measured using these indicators—and the reported smear positive case detection rates for 2008 was studied.

Results: The indicators that were significantly associated with tuberculosis case detection were the following: the proportion of public and private providers outside the national tuberculosis control programme that are engaged in TB control out of existing ones; the sale of anti-TB drugs in the private pharmacies; the positivity rate among TB suspects; The proportion of smear positive TB cases among pulmonary TB cases; Contact management; and proportion of patients subjected to culture and drug susceptibility testing.

Conclusions and recommendations: This tool can assist countries in evaluating their situation, identify gaps, and provide good evidence about the efficiency and sensitivity of their surveillance systems.

TB PROGRAMMES AND CARE: PATIENT PERSPECTIVES

PC-100294-15   The health-disease process from the perspective of patients being treated for tuberculosis

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Background: To know the meaning of tuberculosis patients attribute their health-disease process during treatment.

Methods: Qualitative, exploratory study developed in Capão Redondo, Sao Paulo, Brazil. Data were collected through semi-directive interview in January 2010. Were selected patients reported in 2009, in treatment, over 18 years and without limits of cognition. The empirical data were decoded using the technique of discourse analysis.

Results: The tuberculosis disease remains steeped in stigma, sometimes unnamed. Patients move away from friends and hide their diagnosis from co-workers. Tuberculosis diagnosed causes feelings of panic, agony, anger, worry, depression and discouragement, arising from lack of knowledge of disease and possibility of healing, removal and family disruption to employment. Leads to changes in the habits of the individual, taking care of your health. The condition that promote adherence to treatment: relationship with the health team, desire to cure, treatment credibility, sense of improvement, non-contagious and the provision of free medication. The difficulties for the success of treatment were side effects of medication, uncertainty about the cure, the distance between home and the health service and the need to attend daily to receive medication, long term treatment, and the feeling of improvement in remission symptoms.

Conclusion: Despite advances in diagnosis and treatment of tuberculosis is necessary for the health service to investigate the determinants of adherence to treatment, clearly dependent on the conditions of living.


PC-100563-15   Depression and suicidal tendencies in TB patients

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Background: TB principally affects poor people and worsens poverty. TB may induce depression that can cause immunosuppression and worsen TB. Depression may compound the problems faced by TB patients and impair diagnosis and treatment adherence. We therefore assessed the interaction between poverty and depression in TB patients.

Method: In five Peruvian shantytowns, 135 unselected adult patients recently diagnosed with pulmonary TB answered questionnaires addressing poverty indicators. A poverty scale was constructed based on 5 poverty domains, the scores from which were combined into an overall poverty score that was validated with principal component analysis (97% agreement). The same patients concurrently underwent a psychological assessment, including completing the 21 question Beck depression inventory that has been validated in Latin America.

Results: TB patients had high rates of depression (41%), self-reported suicidal thoughts (24%) and poverty (average per capita income $1.7/day). More extreme poverty was associated with depression ($P < 0.001$) and suicidal ideation ($P = 0.01$), independently of age ($P = 0.1$), sex ($P = 0.4$) and past TB ($P = 0.1$). Specifically, 62% of the poorest third of TB patients were depressed versus 19% of the least poor third of patients ($P = 0.0002$; graph). Considering the five measured domains of poverty: lack of assets ($P = 0.01$) and household crowding ($P = 0.01$)
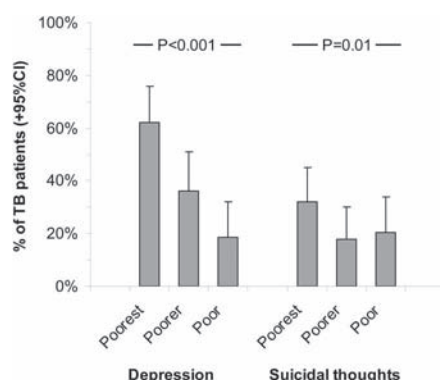
were associated with depression; there was a similar trend for limited household facilities ($P = 0.08$); and depression was not associated with income ($P = 0.9$) or food-spending ($P = 0.2$).

Conclusion: The double challenge of having TB and extreme poverty were strongly associated with depression and suicidal ideation. TB patients living in extreme poverty are much more likely to be depressed or suicidal than patients with better socio-economic resources. Efforts to control TB may be strengthened by integration with activities addressing the despair associated with depression, TB and poverty.

PC-101195-15   Factors determining household costs of tuberculosis and coping strategies in Tajikistan

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Background: Poverty is a cause for tuberculosis (TB) disease, but at the same time one of its consequences. TB patients usually encounter high costs of treatment, even in settings where drugs are provided for free. We investigated factors influencing expenditure levels and risk of impoverishment among TB patients in Tajikistan.

Design: Questionnaire survey with an initial and a follow-up interview of each adult new pulmonary TB case registered over a period of four months in twelve DOTS districts. In a multivariate mixed-effect regression, the main determinants of out-of-pocket payments —either over the whole course of the disease or after enrolment in DOTS treatment—were identified.

Results: Patients and their households faced mean expenditures of US$396 for a TB episode. The main determinant of out-of-pocket payments was receiving additional medication besides the anti-TB drugs. Further important factors were the duration of hospitalization and treatment delay. Sex showed no association with expenditure. To cope with the costs of

illness, two thirds of patients employed a potentially detrimental coping strategy. TB patients raised on average US$23 through credits, US$57 through borrowing money without interest and US$102 through selling assets.

Conclusion and recommendations: Patients in Tajikistan and possibly other post-Soviet countries face catastrophic out-of-pocket payments during a TB episode. This constitutes a high risk for further impoverishment of patients. Mitigation strategies are urgently needed. Case management factors including the common use of additional, symptomatic medication and widespread hospitalization lead to high costs to patients and should be carefully reassessed.

PC-100024-15   Tuberculosis in Iraq: a post-invasion survey of knowledge, attitude and practice in the Anbar Gove

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This community-based cluster study aimed to explore tuberculosis (TB) attitudes, knowledge and practices in Anbar Governorate, Iraq, as well as compares these attributes to a subset of the population with good TB knowledge. Completed surveys were obtained from 692 subjects. 10.6% of these met study criteria for having good knowledge of TB. They were more frequent health care seekers ($P < 0.001$), although also more likely to be dissatisfied with the availability of medicine and equipment at those health clinics ($P < 0.001$). Higher percentages in this Good-Knowledge subgroup felt that TB affected relationships with friends ($P < 0.001$), family ($P = 0.039$) and work performance ($P = 0.036$). Community members from a wide-range of socioeconomic and educational levels require information about TB.

PC-100046-15   Multiple clinics vs. a one-stop shop: patients' experiences accessing TB-HIV care in South Africa

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Background: Efforts to mitigate the TB-HIV co-epidemic are undermined by a failure to integrate TB and HIV healthcare services. Together with clinical complications, the social contexts of coinfection may impede seamless integration of TB-HIV care.

Objective: This qualitative study explored patients'

experiences with coinfection to analyze socio-medical issues related to different levels of TB-HIV service coordination.

Methods: Ethnographic field observations and in-depth interviews were conducted with 27 coinfected patients accessing TB and HIV services at a physically integrated clinic (N1 = 13) and multiple clinics (N2 = 14) in KwaZulu-Natal, South Africa. Data was analyzed through iterative, inductive coding, within a constructivist-interpretivist theoretical framework.

Findings: Emerging themes relating to the double stigma of TB and HIV; social dichotomy of the TB-HIV clinical bond; disparate cultures of TB versus HIV care; and rationalizations related to integrated and non-integrated care, captured how the social contexts of coinfection influenced patients' decisions towards dual healthcare. Qualitative comparisons between patients exposed to diverse degrees of TB-HIV service coordination highlighted their difficulties navigating between multiple clinics, as well as the social constraints of attending an integrated program. While many preferred the one-stop shop TB-HIV clinic model, others preferred to commute between clinics to escape stigmatization and labeling associated with HIV/AIDS. Patients' preferences and participation in integrated care depended on their experiences within the healthcare system, and personal pathways for illness disclosure, acceptance and ownership.

Conclusion: Although integration enables an enhanced response to the co-epidemic, successful programs must consider the social contexts of patients' decision-making for HIV and TB care.

PC-100786-15   TB patients' needs and costs study in Tajikistan

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Background: DOTS implementation began in Tajikistan in 2002. Under the framework of the DOTS strategy, the identification, diagnosis and treatment of tuberculosis (TB) are carried out free of charge. In practice, however, TB patients may not be aware of official treatment policy and experience difficulties due to the burden of related expenses during treatment. The goal of this study was to determine patient need for accurate TB treatment information and full extent of patient costs.

Methods: We used a cross-sectional survey and interviewed 254 TB patients in 9 regions of Tajikistan. We pair-matched urban and rural areas in each of four distinct areas, plus Dushanbe, and randomly selected patients from each region's TB register.

Results: Preliminary analysis of 246 respondents (37.8% female, 58.1% married) showed that 25.2%

did not have enough income for adequate food. Median monthly family income was 300 somoni (~US$69) and total TB-related expenditures were 950 somoni. 72.4% of patients faced costs for services which are officially provided free of charge (mean 142.21 somoni; 95%CI 81.59–202.83). 58.1% of patients reported that expenditures for TB treatment caused significant financial difficulties, and 25.1% reported cost as a reason for delaying diagnosis. While most (88.6%) patients were informed about TB by their physicians, a majority desired more information about treatment. TB education sessions and health providers were the most widely requested avenues of information.

Conclusion: TB treatment entails significant financial expenses for patients. Accurate information about treatment could alleviate the financial burden by making official treatment guidelines known.

PC-100907-15   Patients' perspectives on provision of TB and HIV services in a rural district, South Africa

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Background: The objectives of this study were two-fold: 1) to assess the level of integration of TB-HIV services from patient's perspective, 2) to assess the level of knowledge of ANC-PMTCT clients on TB and HIV transmission, prevention and care.

Methods: The study was conducted from Sept–Oct 08 in Sisonke district in KwaZulu-Natal (KZN). A cross-sectional study was conducted using exit interviews with both TB and HIV/AIDS clients. Ten facilities in the district were selected and a convenience sample of 125 clients was used. Ethical clearance for the study was obtained from the University of the Western Cape and the DOH-KZN research unit and written consent forms were signed by all participants.

Results: A total of 125 HIV clients were interviewed, 80% were females, 20% were males with a mean age of 36.6 years and SD of 10.8, maximum age of 15 years and maximum of 75 years. The majority of the participants (96%) had a CD4 test done, 93.6% were educated on ART, 66% were told about ART adherence. The mean CD4 counts for females (CD4 = 166 leucocytes /ml) was generally higher than males (CD4 = 118 leucocytes/ml).The majority of HIV clients (85.6%) were screened for TB and none of them were screened for IPT. Only 50% of HIV-TB co-infected clients were initiated by the same clinician while 93% of TB-HIV co-infected clients preferred to

be seen by same clinician. Only 36% of participants were knowledgeable about TB symptoms but gender was a highly significant predicator for knowledge levels ($n = 109$, OR $= 2.42$, $P = 0.00$) considering age groups.

Conclusion: the findings of this study suggest that there is a certain degree of integration of TB-HIV services however IPT was not provided to HIV patients with non active TB. Thus suggests a need for provision of IPT. In addition, HIV clients have poor knowledge on TB symptoms thus suggest the need for enhancement of health education programs related to TB prevention and care among HIV patients.

PC-100860-15   The experience of TB patients in London without entitlement to social support

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Background: In the UK, TB medication is free but access to additional resources necessary for treatment completion is conditional. Patients with no recourse to public funds (NRPF), including undocumented and some European Economic Area migrants, have no rights to benefits, public housing or social care. The IUATLD recommends that undocumented migrants with tuberculosis (TB) should receive free treatment and not be deported until completion of treatment. We used case reviews to explore how the IUATLD recommendations translate into current practice in London.

Methods: We reviewed clinical, social circumstances and treatment outcomes for 15 NRPF patients with active TB referred to Find & Treat, a pan-London multi-disciplinary project developed to strengthen TB control in Hard-To-Reach groups.

Results: The case reviews demonstrated that, while TB medication is free, lack of access to public funds severely compromises treatment access, completion and cure. Patients are unable to pay for transport to attend clinic appointments, buy food or access accommodation. Many in fact are sleeping rough. Despite close working relationships with Border Control Agencies, threat of deportation is a reality. Consequences included unsupervised medication, street homelessness, hospital admission (including for malnutrition) and treatment interruption and default.

Conclusion: Lack of clear guidance results in severe inequity of care, and poor treatment outcomes with potentially serious public health implications. Political commitment to provide for basic social needs as well as free medication for all patients is required to effectively control TB. The IUATLD should extend their recommendations to include any foreign national without recourse to public funds.

PC-100900-15   Patients' perspectives on integration of tuberculosis and PMTCT in a rural district, South Africa

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Background: The objectives of this study are two-fold: 1) to assess the level of integration of TB into PMTCT services from patients' perspectives, and 2) to assess the level of knowledge of ANC-PMTCT clients on TB and HIV transmission, prevention and care.

Methods: A cross-sectional study using exit interviews with ANC/PMTCT clients was conducted in Sisonke district in KwaZulu Natal (KZN). Ten facilities in the district were selected and a convenience sample of 150 ANC/PMTCT clients was used and the data was analysed quantitatively. Ethical clearance for the study was obtained from the University of the Western Cape and the DOH-KZN research unit and written consent forms were signed by all participants.

Results: The participants had an average age of 25 years, min age 14 years, max age of 46 years and SD of 6.2. The majority of the participants (73%) were screened for TB symptoms, 57% of them were found to be suspects and only 15% of TB suspects were asked for sputum. The majority (93%) prefer to receive TB treatment at same place. With regards to knowledge on HIV and TB transmission, 62% of the participants knew that being HIV positive you are likely to get TB and 66% participants knew that TB is curable, 96% knew that mixed feeding increases the chances of HIV infection to the baby however there was no statistical significance between age groups ($P > 0.05$). Although 98% of all participants knew they have to test their babies, 85% of those participants aged less than 18 years didn't know and this was highly statistically significant ($P = 0.000$).

Conclusion: The findings of this study suggest that ANC-PMTCT clients were knowledgeable regarding TB and HIV transmission, but that younger patients may have significant gaps in critical knowledge. In addition, there is a degree of integration of provision of TB/PMTCT integrated care, however TB case finding among PMTCT clients is still inadequate. This suggests a need for enhancement of TB screening among HIV pregnant women.

PC-100384-15   The economic impact of tuberculosis among patients attending for treatment in Ethiopia

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Background: The economic burden imposed on TB patients both in the form of direct cost to cover their expenditure on clinical service and indirectly through absenteeism from work, school and other activities is expected to be immense. This problem is not well documented based on the Ethiopian context.

Objectives: To measure the economic burden imposed on tuberculosis patients.

Methods: Cross sectional study undertaken among 419 patients in seven tuberculosis clinics in Gondar, Norther Ethiopia, over four month's period. Information was obtained on direct and indirect patient costs before and after diagnosis, and on financing methods.

Results: It was found that 45%of TB patients were the principal breadwinner of their family and income loss was found to be significant. Direct cost made during illness; 75.6% had paid for examination before and after their diagnosis was made, 77.6% paid for drugs, 46.3% had payment for house rent, and 50.1% had also spent for transport. More than two third were absent from their work for an average of 4–5 months. The mean income lost during this period was 241 ± 524. Expenditures were most frequently financed from selling household assets, taking loan from friend, and using their savings and relatives. Direct and indirect expenditure in half of the patients was found to be more than their annual income and it costs them to sell their asset.

Conclusion: TB Patient had significant direct and indirect cost for TB treatment, which will have impact on treatment and compliance among patients

VACCINES AND DRUG DEVELOPMENT

PC-100035-15   A novel therapeutic vaccine against tuberculosis using the cynomolgus monkey model

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Aim: Multidrug-resistant (MDR), especially extremely drug resistant (XDR), *Mycobacterium tuberculosis* (M. TB) is a big problem in the world. We have developed a novel TB therapeutic vaccine (HVJ-E/HSP65 +IL-12 DNA).

Methods: DNA vaccine expressing TB heat shock protein 65 and IL-12 was delivered by the hemagglutinating virus of Japan (HVJ)-envelope. M. TB was intratracheally instilled into cynomolgus monkeys and then treated with the vaccine.

Results: This vaccine provided remarkable protective efficacy in mouse and guinea pig models compared to the BCG vaccine on the basis of C.F.U of number of TB, survival and CTL activity. This vaccine also provided strong therapeutic efficacy against MDR-TB and XDR-TB in murine models (prolongation of survival time and the decrease in the number of TB in the lung, liver and spleen). Furthermore, we extended our studies to a cynomolgus monkey model, which is currently the best animal model of human tuberculosis. BCG priming and HSP65+IL-12/HVJ vaccine (booster) by the priming-booster method showed a synergistic prophylactic effect in the TB-infected cynomolgus monkey (100% survival). In contrast, 33% of monkeys from BCG Tokyo alone group were alive. Furthermore, this vaccine exerted therapeutic efficacy (survival and immune responses) in the TB-infected monkeys. The vaccine provided therapeutic efficacy of the significant prolongation of survival time (100% survival), the increase in the body weight, and the statistically significant augmentation of proliferation of peripheral blood T-cell from monkeys treated with this therapy.

Conclusion: These data indicate that our novel vaccine might be useful against *Mycobacterium tuberculosis* including XDR-TB and MDR-TB for human therapeutic clinical applications.

Co-workers: Nishida Y, Nakatani H, Takao K, Kishigami C, Nishimatsu S, Sekine Y, Inoue Y, Nagasawa T, Yoshida S, Matsumoto M, Dela Cruz E C, McMurray D, Sakatani M.

PC-100094-15   Induction of monocyte apoptosis by Moreau BCG is TNF-, but not IL-1B-dependent in healthy volunteers

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Background: Tuberculosis (TB) remains the world's leading cause of mortality due to a single pathogen. For its control, studies of TB vaccines are needed. Since BCG is the only vaccine against TB currently in use, studies addressing the protective role of BCG is urgent required.

Methods: Two cohorts of HIV-negative voluntaries have been enrolled for mononuclear cell purification: Control Donors (CD; $n = 8$) and Umbilical Vein (UV; $n = 5$). BCG Moreau RDJ was used for in vitro monocyte infection at 24h and 48h. Annexin V-FITC and Propidium Iodide were used for apoptosis detection in a flow cytometry approach. Supernates were used for TNFα, IL-1β and Matrix Metalloproteinase-

9 (MMP-9) detections by ELISA. Both MMP-2 and MMP-9 were also detected by zymography. *P* levels were setup at < 0.10.

Results: The vast majority of the world's current population has been vaccinated with BCG, with the possible requirement for a booster immunization in adulthood for TB protection. BCG Moreau RDJ strain induced higher apoptosis levels in the CD group only. Soluble factors were released during cell death induction, and TNFα seems to play a critical role since higher levels were also observed in CD-derived monocytes only. On the other hand, IL-1β levels were high in both groups of individuals, but MMP-9 was not dependent on BCG infection and only produced by the CD group. The zymography did not show any major discrepancy.

Conclusion: Here, sustained data have shown an enhancement of in vitro apoptosis in the monocyte population during short-term incubation with BCG Moreau RDJ. This was followed by higher soluble factors released in the CD group, but not in naïve individuals. These preliminary results suggest that induction of monocyte apoptosis by BCG is TNF-α, but not IL-1β-dependent in the BCG-primed group. Therefore, a booster immunization with BCG may protect the immunized individuals and further studies are needed to better evaluate these findings.

PC-100305-15   Bactericidal activity of 2-nitroimidazole against the active replicating stage of *Mycobacterium bovis*

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This study evaluated the antituberculous potential of 2-nitroimidazole under in vitro conditions. Minimal bactericidal concentrations of the compound against actively replicating *Mycobacterium bovis* BCG and *Mycobacterium tuberculosis* H37Ra were found to be 0.226 µg/mL and 0.556 µg/mL in enriched and minimal medium, respectively. Minimal inhibitory concentrations were > 100 times lower than reported antituberculous nitroimidazoles such as nitrofurantoin and furaltadone, indicating the greater potential of 2-nitroimidazole. No discernible effect of 2-nitroimidazole was seen on saprophytic *Mycobacterium smegmatis* and the representative bacterial strain Escherichia coli DH5α, indicating the specificity of the molecule against tuberculous mycobacteria. The compound was also found to be effective against *M. tuberculosis* in the intracellular environment of the human monocytic cell line THP-1, with a reduction in viability of bacilli by 2.5 log after 144 h of incubation at a concentration of 0.113 µg/mL. A five-fold higher concentration (0.565 µg/mL) of 2-nitroimidazole sterilised the macrophages of intracellular pathogens within 192 h, without affecting the host.

However, 2-nitroimidazole was unable to affect significantly the viability of dormant non-replicating bacilli of *M. bovis* BCG and *M. tuberculosis* in Wayne's in vitro model. Overall, the results indicate that 2-nitroimidazole is a potent antituberculous agent active against the organism's active replicating stage, with promising intracellular efficacy as well.

PC-100512-15   Whole blood bactericidal activity of multiple ascending doses of PNU100480

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Background: PNU-100480 (PNU) is a linezolid (LZD) analog with superior efficacy in the mouse TB model, the basis of which is not well understood. This on-going multiple ascending dose study used an ex vivo *Mycobacterium tuberculosis* intracellular infection model to compare the whole blood bactericidal activity (WBA) of PNU to LZD in healthy volunteers.

Methods: Subjects (5–8 per arm) received either PNU BID (100, 300, or 600 mg), PNU QD (1200 mg), LZD QD (300 mg), or placebo for 14 days. Blood was sampled intensively on day 14 for PK and WBA determination. WBA was measured as change in viability in 72 hr whole blood cultures, and reported as $\triangle\log_{10}$/d. Cumulative WBA/d was calculated as AUC. Negative values indicate killing.
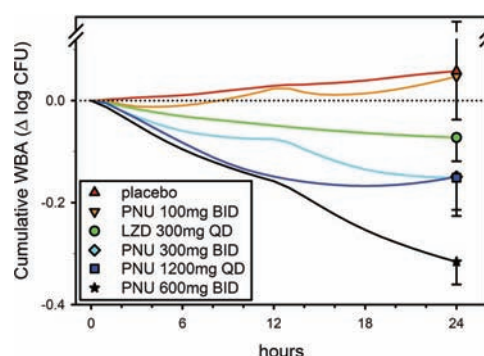
Results: Cumulative growth of $+0.152 \pm 0.058$ per day occurred in placebo recipients. Growth was reduced to $+0.047 \pm 0.085$ by PNU 100 mg BID. PNU 600mg BID resulted in optimal cumulative killing (-0.316 ± 0.044), whereas PNU 300mg BID and LZD 300 mg QD showed intermediate activity $(-0.151 \pm 0.075$ and -0.072 ± 0.046, $P < 0.001$ by ANOVA). Both PNU and LZD exhibited time-dependent killing, reaching 90% of maximal WBA at $2 \times$ MIC, with little additional effect up to $8 \times$ MIC. The inferiority of LZD to PNU was due to reduced maximal effect $(-0.157 \pm 0.051$ vs. -0.424 ± 0.045, $P < 0.001)$ rather than inadequate drug levels. PNU 1200 mg QD showed partial activity $(-0.149 \pm$

0.065) which reflected sub-optimal drug levels starting 12 hr post dose and partial *M. tuberculosis* regrowth starting 18 hr post dose.

Conclusions: This study confirmed the superior efficacy of PNU vs. LZD, which reflects intrinsic differences in bactericidal activity against intracellular *M. tuberculosis*. Optimal PNU regimens may require BID dosing to maintain levels above $2 \times$ MIC throughout the dosing interval. The whole blood model can provide important insights into the PK/PD relationship in TB and accelerate early TB drug development.

PC-100801-15   Clinical research training for upcoming TB vaccine trials in Siaya, Kenya, using a network of sites

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Aim: Lack of research skills is an impediment to clinical trials site development. This deficit may result in inadequate explanation of studies to participants, potential risks for ethical violations and suboptimal data quality. Within a TB-vaccine site development project at KEMRI/CDC in Kisumu, Kenya, funded by EDCTP and Aeras, we established Tiegruok Professional Development Program (Tiegruok) in 2007 to address this shortfall.

Methods: Tiegruok has 3 staff. Training methods include: a train-the-trainer model to deliver pre-existing basic training modules shared by Aeras that covered: Clinical Infectious Diseases & Epidemiology and Biostatistics. clinical research courses, specialty trainings and visits within TB Vaccine Network (TBVACSIN) sites. Pre-tests/post-tests administered for modules/courses and practical assessments of specialty training evaluate staff performance.

Results: Evaluation of clinical research knowledge revealed that epidemiology and biostatistics knowledge were significantly greater on post-test than pre-test (Means: Pre-test = 60%. Post-test = 86%; $P <$ 0.001). Tiegruok together with study coordinators visited partner sites for orientation and familiarization with their activities. Specialty trainings have included: Training in conventional lab techniques for 4 lab staff at San Rafaele Laboratory, Italy; mantoux administration for 9 clinical staff, 7 clinical staff trained to read chest radiographs and 18 trained in sputum collection. The Vienna School of Clinical Research delivered 6 courses including to ~150 participants that included partner sites.

Discussion and conclusion: Staff training and development, if embedded within clinical research, may contribute towards bridging the gap in developing countries' ability to conduct clinical trials.

PC-101513-15   Pharmacodynamics of PA-824 activity in murine TB

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Background: PA-824 is in Phase II clinical trials for TB. It has bactericidal and sterilizing activity in mice. In humans with TB, PA-824 had substantial early bactericidal activity (EBA) in a dose range from 200 to 1200 mg, but no dose-response effect was observed. We evaluated the pharmacodynamics (PD) of PA-824 in murine TB and simulated PD parameters using human pharmacokinetic (PK) data to clarify the relationship between PA-824 concentrations and anti-TB activity.

Methods: Serum Pa PK was determined in mice for doses ranging from 3–1456 mg/kg. Beginning 2 weeks after aerosol infection with *M. tuberculosis* H37Rv, mice received total PA-824 dosage ranging from 144 to 4608 mg/kg over 24 days, divided into individual doses given every 0.5, 1, 2, 3, 6 or 8 days. Lungs CFU counts were assessed 4 days after the last dose. PK analyses and simulations were performed using mouse and human serum PK data and PA-824 MIC values from the EBA trial.

Results: PA-824 PK was dose-proportional from 6 to 243 mg/kg. Individual doses were limited largely to this range. CFU counts at the end of treatment correlated closely with free drug time above MIC (T > MIC) ($r^2 = 0.86$). AUC/MIC had a lower correlation ($r^2 = 0.60$). There was no correlation with Cmax/MIC ($r^2 = 0.09$). T > MIC values associated with bacteriostasis and a 1 log kill were 22% and 48%, respectively. Human simulations estimated T > MIC of 68% for the 200 mg dose, which was associated with 80% of the maximum predicted kill of ~2 log. Doses ≤100 mg were not predicted to have bactericidal activity.

Conclusions: PA-824 has time-dependent bactericidal activity in this murine TB model. Our comparative PD analysis supports the EBA observed with doses ≥ 200 mg in humans and lack of dose response between 200 and 1200 mg/day. Further, it predicts that a dose response will be observed in the ongoing EBA study with daily doses between 50 and 200 mg.

PC-101517-15 Contribution of potent fluoroquinolones and pyrazinamide to second-line regimens in murine TB

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Background: Fluoroquinolones are cornerstone drugs in 2nd-line regimens. In humans, high-dose levofloxacin (L), 1000 mg/day, has early bactericidal activity similar to moxifloxacin (M) 400 mg/day, but is less expensive and more widely available. Pyrazinamide (Z) has a key role in shortening the 1st-line regimen, but is not used beyond the initial phase. The role of Z in 2nd-line regimens lacking rifampin (R) is not well defined. Starting with an idealized 2nd-line regimen of M, ethionamide (E), Z and amikacin (A), we hypothesized that (i) substitution of L for M would not reduce its efficacy, and (ii) use of Z beyond the first 2 months would shorten the treatment needed for cure.

Methods: Beginning 2 weeks after aerosol infection with 4.5 log CFU of *M. tuberculosis* H37Rv, when lung CFU = 7.64 log, controls received 2 months of isoniazid (H), R and Z, followed by HR. Test mice received 2 months of MEZA followed by ME or the same regimen with (i) substitution of L for M and/or (ii) use of Z for the duration of treatment. H, R, Z, M, L, E, and A doses were 10, 10, 150, 100, 300, 50, and 100 mg/kg. Lung CFU counts and relapse rates were assessed for up to 7 months of treatment.

Results: See the Table for lung CFU counts. Relapse rates were 23%, 97% and 100% after 5 months, 0%, 59% and 79% after 6 months, and not done, 20% and 38% after 7 months of treatment with 2RHZ/4RH, 2MEZA/4MEZ and 2LEZA/4LEZ, respectively. All regimens had similar activity over the first 2 months, but the first-line regimen had superior sterilizing activity. Next best were regimens in which Z was given throughout, which cured most mice in 7 months. Use of Z for only 2 months delayed time to culture-negativity. Replacing M with L reduced the activity further in the absence of Z.

Conclusions: 2nd-line regimens including a potent fluoroquinolone, aminoglycoside and Z have sterilizing activity and may be capable of curing TB in far less than 18–24 months if Z is active and used throughout treatment.

Regimen	Mean lung CFU count after treatment for:				
	2 months	4 months	5 months	6 months	7 months
2HRZ/4HR	2.95	0	0	0	not done
2MEZA/3ME	3.11	1.89	1.00		
2MEZA/5MEZ	3.11	0.73	0	0	0
2LEZA/3LE	3.20	2.91	2.27		
2LEZA/5LEZ	3.20	1.19	0	0	0

POSTER DISPLAY SESSIONS

CHILDHOOD TUBERCULOSIS

PS-100377-15 Diagnosis of tuberculosis in children

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Background: During the last decade of the 20th century the number of new cases of tuberculosis (TB) in children increased worldwide. In most children, TB diagnosis is based on diagnostic criteria including positive tuberculin skin test, evidence of TB on chest X-ray or chest CT scan, positive bacteriology and a history of contact with adult TB patients. Polymerase chain reaction (PCR) is one of the newer methods of diagnosis. One of the recent advances in TB diagnosis is measurement of interferon-gamma. The aim of this study was to evaluate bacteriological specimens from children with TB hospitalized in the pediatric, Tuberculosis ward of Masih Daneshvari Hospital between 2001 and 2006.

Materials and Methods: A descriptive study was performed on 126 medical records of children with TB during a 5-year period. Demographic data including age, gender, pulmonary and extra-pulmonary TB presentations, gastric washing smear and culture and PCR were collected.

Results: 126 patients were divided into three groups of age 0–5 yrs, 6–10 yrs and 11–15 yrs, respectively. The highest frequency (68.3%) was observed in the 11–15 year group. 47.6% of the patients were male and 52.4% were female. The tuberculin skin test was positive in 73% of the patients. Gastric aspirate smears, culture and PCR were positive for *Mycobacterium tuberculosis* in 55.6%, 58.7% and 53.2% of cases, respectively. Computed tomography (CT) scan showed evidence of TB in 94.4% of the patients. In 34 patients the chest X-ray was normal and TB was diagnosed via CT-scan of the lung.

Conclusion: The present study suggest that gastric lavage smears and cultures have high diagnostic value in TB diagnosis in children. In addition chest CT-scan is recommended for diagnosis of TB in suspected children when other evaluations are normal.

PS-100148-15   QuantiFERON® Gold-IT Assay vs. tuberculin skin test for the diagnosis of TB infection in Indonesian children

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Background: Children infected with *Mycobacterium tuberculosis* have relatively high risk of progression to disease. The tuberculin skin test (TST) for detection of latent *M. tuberculosis* infection is problematic. We compared the performance of the QuantiFERON® Gold-In-tube assay (QFN) to the TST in Indonesian child contacts of TB cases.

Methods/design: Child contacts of TB cases and age and sex matched healthy community control children were recruited. The QFN and TST tests were performed and results compared across a gradient of exposure. Child contacts over five years of age were re-tested after three months to assess test conversion and reversion rates. Test concordance and discordance were estimated using the kappa statistic and McNemar's test.

Results: In 300 child case contacts test positivity was 49% and 49% for QNF and TST respectively, versus 30% and 14% in 75 community controls. Thus, for both, test positivity increased with increasing exposure. Overall test agreement was 80.0%, discordance was not significant ($P = 0.52$). Agreement varied by exposure level largely driven by the relatively high proportion of QFN positive community controls. Conversion and reversion rates at three months were 23% and 15% respectively for QFN and 20% and 0% for TST.

Conclusion: The QFT test performs similarly to the TST in Indonesian child contacts of a TB case, being at least as sensitive but there is evidence that it is less specific when community controls are tested. Early QFN test reversion is significant and indicates that a negative test should be regarded with caution.

PS-100714-15   Utilisation of tuberculin skin testing in tuberculosis intensive case finding in HIV-infected children

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Background: Diagnosis of active TB infection in HIV-infected children remains a challenge. Tuberculin skin testing (TST) is a cheap and simple tool that may remain useful in diagnosis of TB as part of a simple algorithm for intensive case finding. However, concerns of anergy in the immunosuppressed and false positives in populations vaccinated against TB have limited its use.

Design: HIV-infected children age 6 weeks–14 years within a prospective cohort study evaluating prevalence of TB at Family AIDS and Education Services (FACES) clinic in Kisumu, Kenya were screened for active pulmonary TB. TB was diagnosed according to WHO criteria. Participants were given 0.1 mL of 5TU of purified protein derivative intradermally on the dorsal surface of the forearm. Induration was measured after 48–72 hours. A positive TST was defined as >5 mm. Analysis was done using χ^2 significance testing and logistic regression performed in STATA.

χ^2	TST Results		P value
	Negative	Positive	
TB status			<0.001
No TB	190 (96%)	22 (65%)	
Active TB	7 (4%)	12 (35%)	
CD4%			0.85
<15%	25 (13%)	6 (17%)	
15–<20%	13 (7%)	3 (9%)	
20–<25%	25 (13%)	4 (12%)	
≥25%	130 (67%)	21 (62%)	
WHO Stage			<0.01
1	33 (16.8%)	2 (5.9%)	
2	67 (34.0%)	8 (23.5%)	
3	82 (41.6%)	18 (52.9%)	
4	15 (7.6%)	6 (17.6%)	
BCG			0.5
Parental report			
Yes	199 (93.4%)	34 (94.4%)	
No	14 (6.6%)	2 (5.6%)	
Scar			
Yes	173 (81.2%)	29 (80.6%)	
No	40 (18.8%)	7 (19.4%)	
Malnutrition			0.2
Z-score 0+	115 (54.0%)	20 (55.6%)	
−1	67 (31.5%)	12 (33.3%)	
−2	22 (10.3%)	3 (8.3%)	
−3	6 (2.8%)	0	
ART status			0.2
Yes	180 (84.5%)	33 (91.7%)	
No	24 (11.3%)	3 (8.3 %)	

Multiple Logistic Regression	OR (95%CI)
TB status	14.8 (5.3–41.5)
WHO Stage 3 or 4	
Reference category Stage 1 or 2	2.5 (1.1–5.4)

Results: Of 249 HIV-infected children assessed, 36 (14.5%) were TST positive and 19 (7.6%) were diagnosed with active TB. Mean age was 80 months (SD 40.6) and mean CD4% was 29% (SD 11%). The most common WHO stage was 3 (43.3%) and 86% were on antiretroviral therapy (ART). For those with a positive TST the average induration was 13.9 mm (5–25 mm). WHO Stage 3 or 4 was associated with 2.5-fold increased odds of a positive TST (95%CI 1.1–5.4). Active TB was strongly associated with a positive TST (OR 14.8, 95%CI 5.3–41.5), while

CD4% category was not ($P > 0.8$). Likewise, TST results were not associated with history of BCG vaccination ($P = 0.5$), malnutrition ($P = 0.1$), or use of ART ($P = 0.1$).

Conclusions: Despite concerns regarding the utility of TST in HIV-infected children, these results demonstrate a high rate of positivity even in those with advanced disease and regardless of CD4, BCG vaccination, or malnutrition. The utility of TST as part of TB screening and as a tool in the diagnosis in this high-risk population should be further explored.

PS-101375-15   TB-HIV co-infection among Kenyan children receiving care at a referral hospital

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Background: Little is known about prevalence of TB-HIV co-infection among Kenyan children, or experiences of anti-TB therapy in a setting of ART.

Methods: A retrospective review of clinical information on HIV infected children receiving care in our comprehensive HIV care clinic between 2005–2007 at the University of Nairobi teaching hospital (Kenyatta National Hospital).

Results: Among 697 HIV infected children enrolled in care, TB was diagnosed in 109 (16%) of these children either at (16.5%) or after (83.5%) enrolment. Fifty-seven percent were male and 70% were under 5 yrs. The median CD4 count before anti-TB therapy was 322 (range 3–2991), with the majority of children presenting with immunosuppression. At baseline among children under 5 years, weight for height Z Score (WHZ) fell below −2 in 11 (21.6%) of 51 children with median baseline WHZ of −1.13.

Outcomes: Among 66 children who completed anti-TB therapy, by cut-off date of this analysis, median CD4 increased to 805 (6–3974, $P < 0.001$), median WHZ increased to −0.03, and the proportion with acute malnutrition decreased to 6.9%. Three (4.5%) children developed moderate-severe anaemia (Hb < 8.5 g/dl) while on dual anti-TB/ARV therapy and only one child with Hb < 7.5 g/dl had to stop ART. There was no case of severe hepatoxicity seen. During anti-TB therapy 21 (19%) children were hospitalized and 17 (16%) reported missing doses of ARV during concurrent antiTB/ARV treatment. By date of analysis, 14 (12.8%) children were no longer on follow-up at KNH as follows: 2 (1.8%) died, 4 (3.7%) were transferred to continue care at other sites and 8 (7%) were lost to follow-up.

Conclusions: TB-HIV co-infection is prevalent, and children present with immunosuppression and acute malnutrition. Dual antiTB/ART is well tolerated and results in good treatment outcomes as reflected by improved CD4 counts, improved nutritional status and low mortality.

PS-100096-15   A mobile field site as a model for enrolment and follow up in a tuberculosis incidence cohort in adolescents

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Aim: Adolescents are expected to be a critical target population for new TB vaccine candidates. An optimized approach to enroll both in- and out-of school adolescents in clinical trials is needed to maximize participation and adherence to study procedures. We are conducting a TB incidence cohort study targeting 5000 adolescents aged 12–18 years in an area under continuous health demographic surveillance (HDSS), using a mobile field site (MFS) approach. We report on our experiences with this approach.

Methods: The HDSS facilitates the identification of potential subjects. After consenting and assenting, all parents and adolescents are invited to the centrally located MFS for enrollment baseline evaluations and follow up activities including clinical procedures. The site comprises tents as workstations, a mobile generator, mobile chest X-ray truck and data capture equipment.

Results: Between August 2008 and August 2009 we enrolled 5004 (90.3%) out of 5541 adolescents approached to participate. Of these 95.1% came for the mantoux reading within 4 days. Of 5004 participants 1777 (35.5%) were TB suspects of whom 1725 (34.5%) had chest radiography done, 100% gave the first sputum sample and 94.7% also the second required sample. Over 86.3% completed the first 4 monthly follow up visits while 78.5% month 8 visit and 77.4% month 12 visit.

Discussion and conclusion: So far participation in the study, adherence to study procedures and retention have been high. The MFS eliminates the need of taking participants to hospitals and ensures that the research services are more accessible to community.

PS-101008-15   Clinical experience of tuberculosis in children and adolescents in the maternal and child hospital

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Introduction: Tuberculosis in Bolivia is currently a major public health problem, the present retrospective study was conducted in the Maternal and Child Hospital in the city of La Paz, reviewed medical records of patients who were treated for tuberculosis in a period of 10 years (2000–2009) were identified 277 patients with TB are of which 264 are for patients

with pulmonary tuberculosis, 59 cases with extra pulmonary tuberculosis and 13 cases with pulmonary and extra pulmonary tuberculosis. 24 (8.6%) cases were culture-positive pulmonary tuberculosis in gastric lavage and sputum sample, was identified a case of congenital tuberculosis identified at 40 days old. We did not identify HIV patients.

Objective: To know the experience of cases treated by pulmonary and extra pulmonary tuberculosis in the Mother and Child Hospital in a period of 10 years.

Methods: The patients studied have recorded information: a physical examination, clinical and radiological symptoms of tuberculosis, respiratory symptoms, contact information with TB patients, the origin of the patients studied are in 260 (93%) of area migrant children rural places with high incidence of tuberculosis, with identified risk factors such as malnutrition, anemia, and illiterate parents. We did not conduct the Mantoux test.

Results: Of the 277 patients, 127 (45.8%) were women and 150 (54%) males. Recorded the most frequent symptoms include cough, fever, night sweats, inchazon glands, decreased appetite and activity, weight loss and difficulty breathing. It was identified that 153 (55.2%) of the cases were adult patients contact with pulmonary tuberculosis, 13 (4.6%) had extra pulmonary tuberculosis confirmed by culture, there were 15 (5.4%) tuberculosis meningitis, 12 (4.3%) of osteoarticular tuberculosis, 10 (0.36%) peritoneal tuberculosis, 5 (1.80%) miliary tuberculosis, 5 (1.80%) pericardial tuberculosis, 5 (1.80%) lymph node tuberculosis, 4 (1.4%) tuberculomas, 2 (0.72%) of laryngeal tuberculosis.

PS-101468-15   Tuberculosis amongst children and young adolescents in Siberia, Russia: a cross-sectional study

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Background: The Russian Federation is one of the 22 tuberculosis (TB) high-burden countries in the world, with high rates of drug resistant TB in particular. Nearly 4500 children are diagnosed with TB annually, but little is known about epidemiology and control of TB in children and young adolescents in Russia. This pilot study forms part of a new German-Russian partnership against childhood TB.

Methods: A cross-sectional descriptive study was conducted in Novosibirsk and Tomsk Oblast, Western Siberia. We enrolled all children (0–14 years) and young adolescents (15–18 years) who received TB treatment at any time between August and October 2008 in paediatric TB health-care institutions. Demographic, epidemiological, clinical and diagnostic data were systematically collected from patient file review.

Results: 108 children and young adolescents were enrolled; male 49 (45%). At least 1 BCG vaccination was documented in 90 (83%) cases, of whom 23 had been re-vaccinated. The majority (83; 77%) were detected via active radiological screenings (57; 53%) or via contact investigation (26; 24%); 34 individuals were completely asymptomatic. Close contact with a TB index case was documented in 65/108 (60%). Bacteriological confirmation was achieved in 18 cases (17%). Diagnosis of the remaining 90 TB cases was based on clinical and radiological criteria; 24 were classified as extra-pulmonary TB. Drug-susceptibility test (DST) results were available for 12 of 14 culture confirmed cases; 8/12 (67%) were found to be poly- or multidrug-resistant.

Conclusions: The vast majority of TB cases in children and young adolescents in Russia is currently identified via radiological (fluorography) screenings and contact investigation. Many of those cases are asymptomatic. The proportion of poly- and MDR-TB among individuals with available DST results is high, suggesting extensive transmission of drug-resistant strains in these communities.

PS-100982-15   Trends of new case detection and treatment outcome of paediatric tuberculosis

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Objectives: 1) To describe trends of new case detection and treatment outcome of pediatric tuberculosis under Revised National Tuberculosis Control Programme of Pimpri Chinchwad Municipal Corporation, Pune, Indi; 2) To find out referral pattern of new tuberculosis case detection.

Methodology: The study was based on secondary data such as quarterly performance report, TB register and referral letters of Private medical practitioner (PMP). For trends of new case detection and treatment outcome, study period is confined to 2003–2007 while it was from January to June 2009 to find referral pattern by various sectors.

Results: Proportion of new pediatric (age 0 to 14 years) tuberculosis cases among the cohort of patients is less 5–6% (expected is between 10–15%). New Smear Negative (NSN) case detection has increased 10– 11.4% while New Smear Positive (NSP) case detection has declined from 3.5% to 1.7%. New Extra Pulmonary pediatric tuberculosis case detection has risen from 5.8% to 8.9%.

The treatment success rate have been high and remained above 90 percent for all new types of pediatric tuberculosis. Analysis of referral pattern reveals private sector has contributed 25% to new pediatric TB (age < 15 years) case detection which is less than new tuberculosis cases of age > 15 years (32.9%).

Conclusions: Pediatric tuberculosis should be given priority to improve case detection. Decreased NSP case detection needs further evaluation. It needs efforts to involve more private sector specially pediatricians for better case detection.

PS-100988-15   Resistance of *Mycobacterium tuberculosis* to antituberculous drugs in children under 15 years in Colombia

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Introduction: Tuberculosis is an infectious disease. A third of the world-wide population is infected. Every year nine million cases occurs in the world, one million in population under 15 years old, 719 cases in Colombia.

Objective: Describe the behaviour of *M. tuberculosis* resistant in population under 15 years old in Colombia.

Materials and Methods: *M. tuberculosis* susceptibility tests information related to the drugs from 2001 to June 30th 2009 was analyzed and registered in National Laboratory of Reference of National Institut of Heald. Cases distribution was evaluated by genre, age, disease location, type of sample, TB-VIH co infection, drug resistance proportion.

Results: 128 patients were included, 66 were female (52%) and 62 were male (48%). Age group from 0 to 5 years old were 59 cases (46%), 21 cases from 6 to 10 years old (16%) and 48 cases from 11 to 14 years old (37.5%). The types of disease were 89 (69.6%) pulmonary, 34 (26.4%) extrapulmonar, 5 (39.4%) cases without data. TB-VIH coinfection cases were 7 (5.4%). 125 (97.6%) not treated cases and 3 (2.34%) cases previously treated. Global resistance among not treated cases was 20.8% and MDR-TB was 3.2%.

Conclusion: This analysis demonstrates that exist weaknesses in the fulfillment of the rules impeding the diagnosis and the identification of resistance standards in people under 15-year-old, this is a topic in which it is necessary to explore more.

PS-101371-15   Childhood tuberculosis in a tertiary level referral hospital of Bangladesh

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Introduction: National tuberculosis control programme with its NGO partners have shown much successes in smear positive case management in Bangladesh. The status of child Tuberculosis is not much known in Bangladesh. BRAC an NGO under collaboration with NTP expanded TB services to specialized hospitals. These hospitals are diagnosing many tuberculosis cases including extra pulmonary, smear negative and also child TB.

Objectives: To explore the clinical characteristics of childhood TB diagnosed in one of the major tertiary level hospital.

Interventions: BRAC and NTP established a DOTS corner in this hospital. Data of tuberculosis patients of 0 to 14 years of age diagnosed this hospital were collected from register of DOTS corner and analyzed. Patients diagnosed from indoor and outdoor of the hospitals were sent to DOTS corner for treatment and referral to their nearby DOTS facility.

Results: Total 439 child TB cases were diagnosed from 2008 to 2009, of them 211 (48%) were male & 228 (52%) were female. Among the total child TB cases 77% cases were extra pulmonary. The most common site of extra pulmonary involvement was lymph node 107 (32%), followed by meningitis 97 (29%), plural effusion, abdominal TB and others. Of the total 439 cases only nine cases were smear positive and 94 cases were smear negative Pulmonary TB.

Conclusion: Strengthening diagnosis of Extrapulmonary TB will also help in child TB diagnosis. Involvement of pediatricians and capacity building of providers at different levels are needed. Research should direct towards improved diagnosis of child cases in resource poor setting.

PS-101454-15   Cost-effectiveness of screening and treatment for TB infection in children in a high-burden setting

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Background: Effective delivery of isoniazid preventive therapy (IPT) to TB-exposed children is a vital component of TB control due to children's high

risk of disease progression. We evaluated the cost-effectiveness of 4 screening strategies for TB infection in children ⩽5 years of age with a household TB contact in a high-burden setting. Strategies included the tuberculin skin test (TST); Interferon Gamma Release Assay (IGRA), QuantiFERON-TB Gold In-Tube (QFT); TST followed by IGRA; and, no test.

Methods: We developed a Markov model to estimate health and economic outcomes of screening strategies; cohorts aged 0–2 years and 3–5 years were followed for 15 years. In the base case, costs and outcomes were both discounted at 3%; cost for batched IGRA testing was used. From a societal perspective, we estimated the cost per life year (LYG) gained and incremental cost-effectiveness ratios (ICERs). We considered IPT uptake, adherence, and toxicity, and risk of re-infection. Sensitivity analysis was performed using alternative assumptions regarding screening and treatment.

Results: For the age groups 0–2 years and 3–5 years, the most cost-effective strategy for screening and treatment was QFT (US$891 per LYG and US$974 per LYG, respectively). Compared to the QFT, the 'no test' strategy was associated with an ICER of US$4299 per LYG for the 0–2 age group, and an ICER of US$1529 per LYG for the 3–5 age group. In both age groups, the TST+IGRA strategies were dominated (i.e. resulted in higher costs and lower effectiveness).

Conclusions: Given increased focus on IPT delivery, TB programs in resource-limited settings with high annual risk of TB infection should consider the cost-effectiveness of IPT screening and treatment. Although a no test strategy is most effective in both age groups, it is most costly. IGRA screening to guide IPT in children ⩽5 years of age in household contact with TB is most cost-effective in a high TB-burden setting.

PS-100499-15   Problem of TB-HIV co-infection in children

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Setting: Epidemiological situation on TB among children in Ukraine remains unfavorable. Increasing number of cases of TB-HIV co-infection is one of the main reasons of it.

Aim: To learn dynamics of indicators of TB-HIV co-infection and peculiarities of this pathology in children in Donetsk oblast, Ukraine, for 11 years.

Methods: Analysis of case histories and statistical data of 88 cases of co-infection in children.

Results: Analysis of 88 cases of co-infection among children in Donetsk oblast for 11 years was conducted. Considerable increase of absolute number of TB-HIV co-infected patients was recorded: in 1998–2001—1 case per year, in 2004–2009—10–15 cases per year. Share of co-infection cases with in all TB cases among children increased from 0.9% to 25.0%. Children under 5 years old were the most vulnerable group. Disseminated forms of TB prevailed. TB in phase of degeneration was revealed in 4 cases. 19 (21.6%) children died; progressive tuberculosis caused death in 12 (63.2%) cases.

Conclusions: 1. Considerable increase of TB-HIV co-infected children is registered during last 11 years. 2. Use of anti-retrovirus therapy in combination with standardized anti-TB treatment during 5 years allowed decreasing of lethality rate from 30% to 7.7%.

DOTS: TREATMENT ADHERENCE

PS-100205-15   Research on treatment compliance and related factors of TB patients under the DOTS strategy in China

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Objectives: To understand treatment compliance and related factors of pulmonary tuberculosis patients in different areas under the DOTS strategy, put forward quality and measure to improve DOTS implementation.

Methods: 1) Selected two eastern, central and western provinces respectively in China, 6 provinces in all, selected representative 2 counties in each province, 12 counties in all. 2) Collected local socio-economic general information, the existing TB control policy documents, regular monitoring report information, etc. 3) Investigated 624 tuberculosis patients by questionnaire. 4) Individual interviews: inquired 82 medical staff and 64 tuberculosis patients.

Results: 1) More than 95.5% of 624 TB patients took the medicine within 3 days after diagnosis confirmed. 2.2% TB patients time of starting treatment exceeded 7 days. 2) Proportion of missing dose of TB medicine was 15.1%, western area reached 31.7%, Main reasons were forgetting (51.7%), some due to busy and lack of money; Less than 6% interrupted treatment. 3) 56.6% (39.8%–71.7%)patients had side effects among 624 TB patients, 70.8% were digestive system uncomfortable, next were dizzy (11.3%), very few were tetter, etc; when occurred side effects, 42.5% contact with Dr. in county TB dispensary, 16.4% patients contact with village Dr. 11.8% contact township Dr. 11.2% just stand by themsleves. 4) 72.8% patients wish taking TB medi-

cine managed by themselves, 11.9% hope having family member to supervise them taking medicine, 11.5% would like to have village doctor observed. 33.8% patients did not care having home visits or not, 16% against the home visits.

Conclusions: Treatment compliance on standardization treatment of TB patients was affected by a variety of factors. To improve patient compliance and quality of care for the treatment of patients, should look on patient's need as the center, explore and adopt different approach on treatment and management in different areas and population.

PS-100214-15   Tuberculosis initial treatment default in primary healthcare facilities in South Africa

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Background: Cases with at least one positive smear should promptly be started on TB treatment (WHO guidelines). A study by Creek (2000) in Botswana showed 26.8% smear-positive TB patients had treatment delay or no evidence of treatment initiation. Initial defaulters are patients documented as sputum smear positive in the sputum register, but not appearing in the TB patient register (Harries 2008). Botha (2008) showed a 17% initial defaulter rate in 13 primary healthcare facilities (PHC) in the Western Cape. This study investigates initial defaulter rates at 132 PHC in South Africa.

Methodology: 132 PHC were visited in 5 provinces. Sputum and TB treatment registers were compared per facility. Every smear positive case in the sputum register was searched for in the treatment register. The initial defaulter rates were determined per facility.

Results: In the Eastern Cape, the range of the initial defaulter rate was 2.8% to 61.9% (mean 20.8%). In Kwazulu-Natal, the range was 0.0% to 66.6% (mean 23.0%). In Limpopo, the range was 0.0% to 75% (mean 23.7%). In Mpumalanga the range was 0.0% to 70.0% (24.1%). In the North West the range was 11.1% to 50.0% (24.1%). The mean of the means initial default rate was 23.1% across provinces, with a range of 0.0% to 70%.

Discussion: This study shows a wide range of initial defaulter rates between and within provinces. The results are of major concern and is an issue that must be addressed urgently by the National TB programme.

PS-101156-15   Red Cross experience on forming adherence to treatment and social support for TB patients

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Setting: Khabarovsk region, Russian Federation.

Objectives: Defaults is the most common challenge of the TB treatment. The main reasons of defaults are alcohol abuse (50% of patients), lack of adherence of TB patients to a long-term treatment (25%) and difficulties with treatment of homeless people (25%).

Since 2005 the International Federation of Red Cross and Red Crescent Societies (IFRC) in collaboration with the Russian Red Cross (RRC), regional authorities and TB services are implementing comprehensive TB program in Khabarovsk region. A critical component of the program has been the provision of social support during the continuation phase of TB treatment.

Methods: During the continuation phase of DOTS, the TB dispensary staff are identifies socially vulnerable groups in need of social support based on predetermined social criteria: average income per capita in the family below the minimum income level in the region; unemployed people; elderly alone people; ex-prisoners; migrants; people from multi-children families; homeless. The social support interventions included food parcels ('protein kits' given daily cost 1 USD/once per two weeks cost 6 USD/once per month cost 17 USD), transport reimbursements, psychology counselling, patients training at 'TB school' and personalized care through organizing convenient DOT.

Results: 3287 people are covered by social assistance during 2005–2009. The results of the treatment showed 7% only of defaults out of 448 TB patients, who were registered in 2008 and received social support against 14% of defaults among 73 TB patients without social support before intervention.

Conclusions: Social support is effectively increase adherence to treatment and significantly reduce the default rates. Experience gained in the Khabarovsk region can be successfully replicated in the other regions of the Russian Federation.

PS-100231-15   Gender differences in adherence to guidelines for evaluation of TB suspects

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Background: The International Standards for Tuberculosis Care (ISTC) recommend that (1) All persons with unexplained cough lasting 2–3 weeks or more should be screened for TB and (2) All patients suspected of pulmonary TB should have at least 2 sputum specimens examined for AFB. We used data from an ongoing infectious disease surveillance project in Uganda to evaluate gender-specific differences in adherence to these guidelines.

Methods: The study included all adults (age $\geq$ 15) evaluated at six Level IV Health Centres between January and December 2009. At each health center, a data assistant entered data on patient demographics, symptoms, laboratory tests and treatment into an electronic database. We compared the proportion of male and female TB suspects evaluated according to the ISTC using hierarchical regression methods.

Results: Of 76 096 eligible patients, 1699 (2.2%) reported having cough for two or more weeks. The median age of these TB suspects was 33 years (IQR 24–48) and 60% were female. Overall, 521 (31%) TB suspects were referred for sputum AFB examination and 421 (80%) completed sputum examination. Female TB suspects were 13% (95%CI 9–17%) less likely than male TB suspects (31% vs. 44%, $P <$ 0.001) to be referred for sputum examination. However, among patients referred, there was no difference (−4%, 95%CI −10% to + 3%) in the proportion of females and males (79% vs. 83%, $P =$ 0.24) who completed sputum examination.

Conclusions: Women with sub-acute cough are less likely than men to be evaluated according to the ISTC. Gender-specific differences in the evaluation of TB suspects should be evaluated and addressed when expanding DOTS programs in low-income countries.

PS-100627-15   Factors associated with default from treatment among tuberculosis patients in Nairobi Province, Kenya

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Setting: Thirty tuberculosis treatment facilities in Nairobi, Kenya.

Objectives: To determine the duration of treatment before default and factors associated with default.

Design: Case-control study of treatment defaulters (cases) and patients who completed treatment course (controls). Primary and secondary data were utilized. Patients whose treatment outcome was between January 2006 and March 2008 enrolled. Response variables were default or completed treatment course. Data was analyzed using SPSS and EpiInfo software. Univariate and multivariate logistic regression analysis to determine association and survival analysis utilizing Kaplan-Meier method were applied.

Results: Total of 945 treatment defaulters and 1033 patients that completed treatment course enrolled (120 cases and 154 controls traced and interviewed). Default occurred most frequently during the first three months of treatment (59.1%). Among initially AFB smear positive defaulters, 47.7% terminated treatment before confirmation of sputum conversion. Ignorance (16.7%), traveling (12.4%), feeling better (11.6%), side-effects (10.7%), herbal medication use (8.3%), alcohol use (7.4%), inadequate food (6.6%), unfavourable facility factors (6.6%) and stigma (5.8%) were major reasons for default. Inadequate knowledge on TB (OR 8.67), herbal medication use (OR 5.7), low income (OR 5.57), alcohol use (OR 4.97), previous default (OR 2), HIV co-infection (OR 1.56) and the male gender (OR 1.4) were independently associated with default.

Conclusion: Default occurred most frequently during early months of treatment. Main reasons for default were ignorance, traveling away from treatment center, feeling better and side-effects. Predictive factors for default were inadequate knowledge on TB, herbal medication use, low income, alcohol use, previous default, HIV co-infection and male sex. Enhanced patient pre-treatment counseling and education on TB is recommended

PS-100634-15   Role of DOTs observers in tuberculosis default in Hasan Sadikin Hospital, Indonesia

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Background: The default number of patients in tuberculosis treatment in 2008 in Hasan Sadikin Hospital Bandung achieved 22% that is much higher than the national standard (<5%). The aim of this study was to explore the role of DOTs (directly observed treatment short courses) observer of tuberculosis patient in Hasan Sadikin Hospital.

Methodology: This case-control study using data

were collected via interview with questionnaires from 79 DOTs observers of default patients (case) and 79 DOT observers of completely treated patients (control) who were systematically randomized, then it was sought the association between the active role of DOTs observers and the failure of the patients to accomplish their tuberculosis treatment.

Results: The study results showed that there was no significant difference between active DOTs observers and inactive DOTs observers based on variables of occupation, distance and cost; statistically, the variables affected the role of DOTs observers to be predictive for default through the role of DOTs observer include the patient's satisfaction to health care service ($P = 0.039$), education ($P = 0.448$), knowledge ($P = 0.322$), and stigma ($P = 4.589$) (Table 1), whereas the role of inactive DOTs observers had a risk 17 times for default compared to that of active DOTs observers (OR 16.933; CI 95% 7.698–37.246).

Conclusion & recommendation: The failure of patients to accomplish the tuberculosis treatment in Hasan Sadikin Hospital can be reduced by regarding the good knowledge, high education, and no stigma belong to the DOTs observer in taking drug. Default can be done improving the quality of hospital services.

PS-100642-15   Community health workers can help achieve good cure rates: experience from Kiambu West, Kenya

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Background: Kenya faces acute shortage of healthcare workers. TB services decentralization becomes a big challenge due to the staff shortage. The country also adopted the community strategy to bring health services to the people. This abstract shows that these community health workers (CHWs) can help deliver TB services and have good treatment outcomes in areas of staff shortage.

Methods: CHWs from the local community were trained on basic TB care and joined a trained nurse who mentored them in TB service delivery and recording updating of TB records. They were then assigned to TB rooms where they do most of the TB services for 2 days a week then the 3rd day trace any defaulters to treatment. They are paid a minimal allowance from the district medical office.

Results: The 5 facilities had very good treatment success for the smear positive (SS+) cases. The cure rates were comparable and even better at times than for facilities ran by trained nurses. The treatment outcomes for the 2008 SS+ cohort were Ndeiya HC 96% ($n = 32$), Wangige HC (85% ($n = 52$), Gichuru Dispensary 86.3% ($n = 16$), Uthiru Dispensary 89 % ($n = 35$), Lari HC (81%). All other indicators were equally impressive and defaulters were very few.

Conclusions: CHWs if well trained, mentored and supervised well can help in delivery of TB services. This element of task shifting can be adopted in developing countries/areas experiencing human resources for health crisis to deliver TB care in rural and remote communities.

PS-100768-15   Analysis of initial defaulters in selected districts in Tajikistan

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Background: The global objective for TB control program is detection of 70% of all existing TB cases and treatment of 85% of them. Resolving the problem of initial defaulters, i.e. the detected SS+ TB patients who did not start treatment for various reasons, is an important step towards achieving these objectives. The goal of this study was to analyze the initial default cases in selected districts of Tajikistan by reviewing completeness of registration of SS+ TB patients detected by microscopy laboratories.

Methods: During routine monitoring visits, we analyzed the registration of new pulmonary SS+ TB cases by cross-comparing the microscopy laboratory register (TB 04) with the TB district register (TB 03). The analysis was carried out for four quarters (Q 3,4–2008, Q 1,2–2009) in the Vose, Temurmalik, Khamadoni and Rudaki districts.

Results: For the abovementioned period in specified districts there were 254 SS+ cases detected and 209 of them were also registered in the district TB register. Out of the 45 unregistered cases, 27 (60%) were inhabitants of other districts. The reasons for non-starting treatment for the remaining 18 unregistered cases were: 2 deaths, 1 refused to start treatment, 1 moved out of the country, and 1 was imprisoned. 13 cases (29%) did not start treatment for unidentified reasons. The worst situation is in Vose rayon where 13 out of 52 detected cases are unregistered (25%).

Conclusion: The analysis revealed two important findings. First, that people are commonly referred to a different district than the one they reside in for a sputum microscopy test, possibly due to stigma (10.6% of detected SS+ cases were residents of neighboring district). Second, among newly detected SS+ cases, who are residents of discussed districts (227), initial defaulters comprise 7.9% (18/ 227) reaching as high as 25% (13/ 52) in the least effective DOTS centers.

PS-100984-15   Is TB cure communicable? Ex-patients' contribution to TB outcomes in DR Congo

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Rationale: Ex-TB patients 'Club des Amis Damien' (CAD) has extended its activities from Kinshasa to new provinces with support from The Union, to contribute to national TB control program (NTP). Our objective is to evaluate ex-patient contribution to TB control outcomes.

Methodology: Binga and Lisala, two neighboring health districts in Equateur province were selected as being comparable and Lisala was randomly selected to benefit from the intervention. From 01/09 onwards, CAD delivered a package comprising of TB suspect identification and referral to TB clinic and peer-provided psychosocial support to patients on treatment. CAD activists trained 20 ex-TB patients to deliver the intervention on the ground of their willingness. This core group was made responsible for delivering the intervention. Supervision was done as normal by the NTP provincial team. We compared case finding and treatment results obtained from NTP statistics before and after intervention at Lisala, and between the two districts. Patients referred and supported were registered by peer volunteers, and peer volunteer registers were compared with TB registers during quarterly NTP reporting to attribute responsibility of outcome to CAD intervention.

Results: In 2009, ex-patient volunteers referred 166 suspects to the 4 NTP-accredited TB centers of Lisala district that detected 83% of the 308 new cases of Sm+TB; the remaining 17% were detected in two centers that did not receive CAD support. 130 (78%) of CAD referred patients were confirmed with sm+TB. These patients represented 50% of the total number (258) of sm+ cases detected by the 4 centers.

	2008	2009
Lisala = Intervention		
Population	239 183	241 575
Nr new Sm+ CAD	0	258
Nr new Sm+ non CAD	151	50
Nr new Sm+ total	151	308
SM+ notification rate /100K	63	127
SM+ success rate CAD, %	0	86
SM+ success rate non CAD, %	85	100
SM+ defaulter rate CAD, %	0	5
SM+ defaulter rate non CAD, %	0	0
Binga = Control		
Population	224 592	226 838
Nr new Sm+ total	122	141
SM+ notification rate /100K	54	62
SM+ success rate, %	82	82
SM+ defaulter rate, %	3	1

Conclusion: Referral by selected peer patients is an efficient contribution to case finding. Further research is necessary to assess the impact of ex TB patient association on the outcome of treatment. The observation of defaulters in Lisala after CAD intervention calls for further exploration of ex-patients involvement in TB reporting.

PS-100423-15   Improving DOTS by involving family members as treatment supporters in Lahore District Pakistan

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Background: Directly Observed Treatment is key component of DOTS. In Pakistan, Lady Health workers (LHW) are doing this job. Coverage of lady LHW is suboptimal, causing low adherence to treatment particularly in urban areas. Purpose of this study was to increase adherence by organising family members (FM) as treatment supporters in setup where LHWs are deficient.

Objective: Improving adherence to treatment by Involving Family Members as treatment Supporters.

Methods: Design; Quasi Experimental study Setting; District Lahore, Pop 9 M. Duration; 9th November, 2009 to 28th February, 2010. Sample size; 120 patients. 60 urban, 60 Rural (30 in urban setting and 30 in rural setting). Patients were selected by purposive non probability sampling from randomly selected 6 Rural Health Centres and 3 Tertiary Care centres. Experimental Group-Family Member DOT (FM DOT); Modular training of Health workers, Family member were selected by patient, given health education, letter of agreement signed by FM, FM monitored by health worker. Control group; Historical community Group under DOTS in Quarter 3, 2009. Data was collected from DOTS Recording Tools.

Results: In urban setting: In Exp Group, all 66 urban patients were adherent to treatment as compared to control group, in which, 298 out of 388 were adherent. $P = 0.000$. In Exp Group, 30 out of 31 rural patients were adherent while in Control, 232 out of 299 were adherent, $P = 0.008$. In Exp group, all
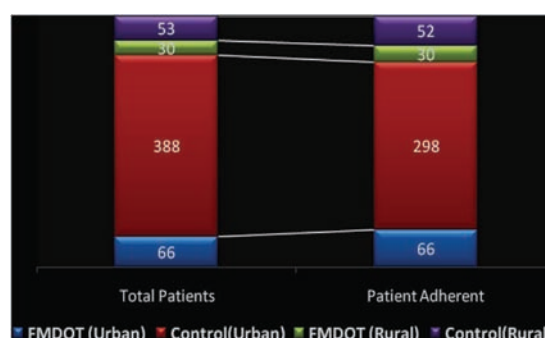
25 smear positive patients were converted to negative while in control 113 out of 246 were converted, $P = 0.01$. In rural setting: In Exp group, all 30 patients were adherent while in Control, 52 out of 53 were adherent, $P = 0.4$. All smear positive patients in Exp and Control groups were converted to negative. **Conclusion:** In urban setting, patients treated under Exp group were significantly more adherent to treatment as compared to control Group, while in rural setting there was no significant difference in both groups.

MDR-TB TREATMENT AND OUTCOME

PS-100025-15   Results of lung resection and pulmonectomies of multidrug resistance of *Mycobacterium tuberculosis*

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Partial lung resections and pulmonectomies were performed in 82 patients (males 56, females 36) at ages between 20 and 40 having fibrous-cavernous pulmonary tuberculosis with Multidrug resistance of mycobacteria. The resistance of mycobacteria towards isoniazid + rifampicin was detected in 8 patients, towards isoniazid + rifampicin + streptomycin in 43, isoniazid + rifampicin + streptomycin + ethambutol in 31. A total of 78 patients (95.1%) were ill with tuberculosis during 2 to 5 years. Long term antitubercular chemotherapy was ineffective due to clinical heaviness of illness, prevalence (in 61.0% of patients) and progressive course of pulmonary tuberculosis (in 46.3%), development of complications—pleural empyema, pulmonary hemorrhage (50.0%). During 2–3 months prior to operations, a complex treatment including pyrazinamide + amikacin + ofloxacin + prothionamide + paraaminosalicylic acid + cyclocerine, pneumoperitoneum, ultraviolet blood radiation, transfusion of albuminous, saline and synthetic solutions, sanation of pleural empyema were carried out. After operations, complication occurred in 27 patients, including bronchial fistula and pleural empyema in 12 (14.6%), pleural empyema without fistula in 2 (2.4%), re-activation of tuberculosis in the operated lung in 13 (15.8%). These complications were eliminated in 19 patients. Good clinical effect of performed operations was established in 73 patients (89.0%), unsatisfactory in 3 (3.7%). A total of 6 patients (7.3%) died from the progress of pleural empyema and cardio-pulmonary insufficiency. The effectiveness of partial lung resections was 92.5%, and that of pulmonectomies, 85.7%. **Conclusion:** At fibrous-cavernous pulmonary tuberculosis with multidrug resistance of mycobacteria, the resources of therapeutic treatment are significantly

limited. Partial lung resections and pulmonectomies are the basic and highly effective methods of treatment and heal 89.0% of operated patients.

PS-100026-15   Results of resection operations at first detected pulmonary TB after ineffective DOTS therapy

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A total of 43 patients with first detected pulmonary tuberculosis (males 27, females 22) in ages between 18 and 53 were receiving chemotherapy according to the 1st and 2nd category of DOTS during 1–1.5 years with unsatisfactory results. Fibrous-cavernous tuberculosis was diagnosed in 41 patient, tuberculoma in 2. Mycobacteria of tuberculosis in sputum were detected in 36 patients (83.7%), of them in 16 (44.4%) with multi- and poly-resistance to isoniazid, rifampicin, ethambutol and streptomycin. The complications of pulmonary tuberculosis (blood spitting and pulmonary hemorrhage, spontaneous pneumothorax and pleural empyema) were observed in 12 patients (27.8%). Just before operation, 23 patients received treatment under the 1st DOTS category during 6–9 months, and 20 patients under the 1st and the 2nd categories consecutively during 1–1.5 years. Ineffectiveness of the treatment under DOTS was the reason for surgical treatment.

Segmental lung resection was performed in 7 patients, lobectomy in 12, pulmonectomy in 24. Good clinical effect was reached in 40 patients (93.0%), unsatisfactory results in 2 (4.7%). One patient died from the progress of post-operative pleural empyema and re-activation of tuberculosis. **Conclusion:** At first detected destructive pulmonary tuberculosis, DOTS chemotherapy doesn't always lead to positive clinical effect. In these cases partial lung resection and pulmonectomy serve as one of important final stages of treatment and heal 93.0% of patients and prevent transition into chronic illness.

PS-100364-15   Medico-social features of patients treated under DOTS-PLUS program with outcome failure

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Background: Last years in the Russian Federation the number of patients with multidrug resistant tuberculosis (MDR-TB) increases promptly. The program DOTS-PLUS started in Tomsk area since September 2000. From September 2000 till September 2008 under program DOTS-PLUS in Tomsk area (Russia) 870 persons have been treated, from them

166 patients (19.08%) had failures in treatment. The purpose of our work is the analysis of the reasons of an inefficiency of treatment at patients suffering from MDR-TB who has been treated under the program DOTS-PLUS.

Methods: For an estimation of mediko-social features at 98 patients case records and out-patient cards of patients which have been treated under program DOTS-PLUS with an outcome failure in treatment have been analysed.

Results: Middle age of patients has made 36.05 years, women have made 26.53% (26) persons, men of 73.46% (72). Analyzing the social status of patients, we have revealed, that only 2.04% (2) patients had work, the others were the unemployed or invalids. Among patients of our group countrymen of 59.18% (58) prevailed, townspeople have made 40.81% (40). From 98 persons in jails earlier there were 37.75% (37). At patients from analyzed group the syndrome of alcoholic dependence was at 70.4% (69), the use of narcotic preparations at 8.16% (8), 89.79% (88) persons smoked, thus the experience of smoking was more than 10 years at 78.83% (77) patients. We have established, that 42.85% (42) patients have previously received anti-TB treatment, 37.75% (37) patients were newly diagnosed and 15.3% (15) the patients with a chronic current of process.

Conclusions: Analyzing the obtained data, we can allocate following mediko-social features of patients with failure in treatment under program DOTS-PLUS: they are mainly jobless men of young able-bodied age living in countryside. Almost 40% of patients happened in imprisonment places. More than 70% of patients had problems with abusing alcohol.

PS-100470-15 The National Multidrug-Resistant Tuberculosis Service

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Introduction: The management of multidrug-resistant tuberculosis is an emerging problem in the UK. The low incidence in the UK means that few specialists treating tuberculosis have much experience of managing patients with MDR-TB and no mechanism for collecting data on the progress and outcomes of such patients exists. To attempt to overcome this gap, the MDR-TB Service was established at the Liverpool Heart & Chest Hospital in January 2008.

Method: The service offers ready access to expert advice on the management of patients with MDR-TB via an electronic virtual committee of TB experts. The advice given offers the likely best treatment for patients and by doing so prevents the emergence of XDRTB. The second function of the Service is to collect data on all MDR-TB cases identified in the UK and record outcomes.

Results: From 2008, the MDR-TB Service has been approached for advice on 77 TB cases. Of these 60 were confirmed as MDR and 4 XDRTB whilst the remainder either could not be confirmed as MDR, were isoniazid OR rifampicin mono resistant or were more general requests for advice.

The initial resistant patterns of sixty MDR-TB cases showed resistance to isoniazid and rifampicin, 53% of the cases were resistant to streptomycin, 43% to ethambutol and 33% to pryazinamide. The majority of the cases were born outside the UK, 56% being from either India (31%) or Sub Saharan Africa (25%). To date two patients are known to have died and the rest are continuing on treatment. 57% of the pulmonary MDR-TB cases were known to be sputum smear positive and therefore infectious.
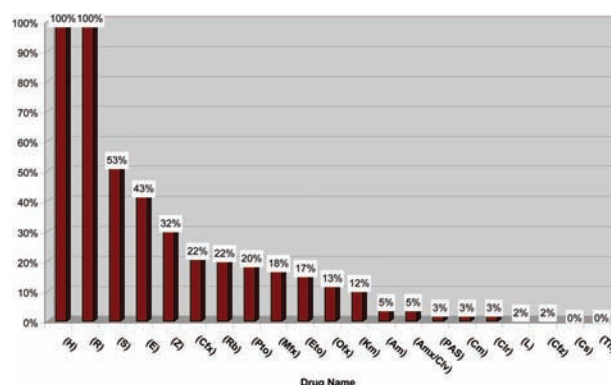

Figure   UK MDRTB drug resistance pattern.

Conclusion: The MDR-TB Service is an important means of providing expert advice on management of these cases. Streptomycin resistance was present in the majority.

PS-100516-15   Is DOT crucial to increase treatment efficacy in MDR-TB?

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Background: The tuberculosis resistant treatment became a major challenge to the tuberculosis control in the world, mainly in the countries with high burden of disease. Scarce information is available for MDR cases.

Objective: This study aims to assess the efficacy of DOT to prevent treatment default to drug-resistant TB in Brazil.

Methods: We analyzed the data of Brazilian Tuberculosis Resistant Surveillance Project. Patients included in this study were admitted for treatments from January 3, 2000, to December 30, 2004. The study population consists of 402 patients from the states of Bahia (7.5%), Para (22.4%), Rio de Janeiro (55.7%) and Sao Paulo (14.4%). Survival analysis was used to evaluate the effect of the treatment strategy and adjusted estimates of rate ratio were obtained. We used Proportional Cox regression model to estimate hazard rate ratios.

Results: A group of 153 patients were submitted to DOT treatment, while 249 used non supervised treatment. They were similar considering male sex: DOT (62.7%), non-DOT (66.2%); age: DOT (mean 38.7 ys) non-DOT (mean 39.5 ys), alcoholism: DOT (2.0%) and non-DOT (2.4%), but the DOT group had more black people (9.8%) than non-DOT one (26.9%). The groups were also similar considering others clinical and laboratory exams feature like the mycobacteriological resistant profile. In DOT group 90.8% had second line drug resistance and 88.8% in the non-DOT group. Aids were present in 6.5% of DOT patients and 4.4% in non-DOT ones. The default rate was 2.6 cases by ten thousand person-day in non-DOT group and only 0.9 cases by ten thousand person-day in DOT group. The hazard rate ratio of default adjusted for sex, age, race, alcoholism and AIDS was 0.37, comparing DOT with non-DOT groups. Among patients not treated with DOT, the treatment default is almost 3 times likely than on those treated with DOT.

Conclusions: DOT reduces substantially the treatment default, so is crucial to increase treatment efficacy in MDR tuberculosis.

PS-100670-15 Drugs logistics management of second-line anti-TB drugs by RNTCP, India: overcoming challenges

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Background and challenges to implementation: Drug logistics of second-line anti TB drugs, required for treatment of MDR-TB patients under DOTS Plus has emerged as a new challenge to RNTCP in India. This is due to the fact that the influx of patients into the Programme is slow, treatment is spread over 24 months and these drugs have shorter shelf life than first-line drugs. Accurate forecasting of drugs is one of the key factors which ensures an uninterrupted drug supply to the patients. Currently, ten states in the country are in the process of implementing the DOTS-Plus programme in their respective areas.

Response of RNTCP: Detailed guidelines for logistics management of second-line drugs have been finalised by the Programme after many consultations and field visits to the concerned sites. Training on drug logistics management to the field staff is done regularly by the states.

Results and lessons learnt: These guidelines have evolved based on initial field experiences and regular consultations with district and state officials. Regular reporting of stock status to higher level is done by sub district, district and state drug stores. As a result, there have been no stock outs of these drugs in the concerned states.

Conclusions and key recommendations: Regular monitoring of drug stocks, trainings to field staff, supervisory visits and consultations with state and district officials have improved logistics of these drugs under RNTCP in India.

PS-100677-15 Risk factors for poor treatment outcomes in Russian MDR-TB patients treated with second-line drugs

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Background: The objective of this analysis was to identify predictors of poor treatment outcomes among multidrug-resistant TB (MDR-TB) patients treated with second-line drugs (SLDs) in Orel and Vladimir Oblasts.

Methods: Consecutive adults with pulmonary MDR-TB were enrolled 01/2007–12/2008. Clinical and microbiological data were recorded at the start of treatment and monthly for 2 years. Death, default, and treatment failure were considered poor outcomes. Prevalence ratios (PR) with 95% confidence intervals (CI) were calculated using multivariate regression analysis to identify statistically significant predictors.

Results: By Feb 2010, 115 patients had reached a treatment outcome as follows: cured 28 (24%), failure 7 (6%), death 18 (16%), default 11 (10%), transferred 5 (4%), while 46 (40%) were still on treatment. In univariate analysis, death/failure (versus cure/continuing treatment) were associated with alcohol abuse (PR = 2.8 (95%CI 1.4–5.4)), being a retreatment case (PR = 2.4 (1.0–5.8)), a history of treatment with first-line drugs (compared to new cases) (PR = 2.8 (1.2–7.0)), having defaulted from previous treatment (PR = 3.6 (2.0–6.4)), cavitary TB disease by chest X-ray (PR = 6.9 (1.0–47.9)), having XDR-TB at the start of treatment (PR = 2.8 (1.5–5.3)), resistance to any SLD (PR = 2.3 (1.0–5.3)), resistance to all injectable SLDs (PR = 2.6 (1.1–5.7)) and resistance to any fluoroquinolone (PR = 2.6 (1.4–5.0)). In multivariate analysis, independent predictors of

death/failure outcome included having XDR-TB at the start of treatment (PR = 3.6 (2.0–6.5)), alcohol abuse (PR = 3.1 (1.7–5.9)), and having defaulted from a previous treatment (PR = 2.6 (1.8–3.8)). Default (versus cure/continuing treatment) was associated with history of TB treatment failure (PR = 4.7 (1.5–14.1)).

Conclusion: Having XDR-TB at the start of treatment, alcoholism and default history predicted death/failure treatment outcome. Default in the current episode was associated with previous TB treatment failure.

PS-100693-15   Third-generation mobile videophone integrated into the DOTS-Plus program in northern Taiwan

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Aim: In order to facilitate the relationship between patients and providers, third-generation (3G) mobile videophones were used to watch selected patients take their medication in DOTS-plus program of northern Taiwan. The aim of this study is to evaluate this novel model of DOT by integration of supporters (S-DOT) and videophones (V-DOT).

Methods: From August 2007 through August 2009, 94 confirmed Taiwanese MDR-TB patients were enrolled into this hospital-initiated DOTS-plus program under the supervision of Taiwan CDC. These patients were allotted to S-DOT group and V-DOT group based on the patients' history of previous anti-TB treatment, cognition of disease, disease severity and sputum status, family support and patient's willingness. In S-DOT group, supporter would visit the patients at prearranged time. In V-DOT group, every patient could call the nurse at prearranged time at anyplace and all pills would be swallowed in view of the 3G mobile videophone. The 6-month sputum culture status and treatment outcome were evaluated on February 28, 2010.

Results: A total of 94 patients aged from 16 to 87 years old were enrolled. Twenty-four patients (25.5%) were allotted as V-DOT group, 59 patients (62.8%) in S-DOT group, 5 patients (5.3%) in mixed V-DOT/S-DOT group and 6 patients (6.4%) in hospital/nursing home group. Assessment of treatment outcome on February 28, 2010, showed 39 patients (41.5%) were cured/treatment completed, 49 (52.1%) had negative sputum culture with expecting to have treatment success, 5 (5.3%) non-TB death and 1 (1.1%) defaulter. Treatment success/expecting treatment success rate was 100% (24/24) in V-DOT group and 96.6% (57/59) in S-DOT group. The 6-month negative sputum culture rate was 100% in both V-DOT and S-DOT groups.

Conclusions: In addition to supporters, 3G mobile videophones could be considered as an alternative modality to watch patients take medication in selected MDR-TB patients.

PS-100735-15   Risk factors and reasons for poor treatment outcome of MDR-TB in Manila, Philippines

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Aim: To identify risk factors and reasons for poor MDR-TB treatment outcome.

Methods: Retrospective review of clinical charts of MDR-TB patients enrolled for treatment in 3 MDR-TB clinics of Manila from July 2003 to October 2005.

Qualitative part: 5 focus group discussions (FGDs): 3 with well adherent and 2 with poorly adherent MDR-TB patients on treatment in 2007 in the 3 MDR-TB clinics of Manila.

Results: Of the 240 MDR-TB patients who had complete records, 76% (n = 182) got cured, 13% (n = 31) defaulted, 10% (n = 23) died and 2% (n = 4)

Risk factors for default and death during MDR-TB treatment	Cured (n = 182)	Defaulted (n = 31)	Died (n = 23)
1 Socio-economic status			
Class A or B	89%	9%	2%
Class C (poor)	76%	12%	12%
	P = 0.045	P = 0.57	P = 0.04
2 Body weight at treatment start			
At least 47 kg (the median weight)	89%	7%	4%
Less than 47 kg	65%	19%	16%
	P < 0.0001	P = 0.007	P = 0.002
3 Diabetes mellitus (co-morbidity)			
Yes	88%	6%	6%
No (no diabetes mellitus)	73%	16%	11%
	P = 0.02	P = 0.04	P = 0.3
4 Resistance to a second-line drug			
No	81%	9%	10%
Yes	72%	19%	10%
	P = 0.08	P = 0.03	P = 1
5 Percentage of missed treatment days over the whole treatment period			
Good adherence (≤2% of treatment days missed)	81%	0%	19%
Average adherence (2.01 to 19.99% of treatment days missed)	82%	10%	7%
Poor adherence (≥20% of treatment days missed)	36%	56%	8%
P-value (2 degrees of freedom)	P < 0.0001	P < 0.0001	P = 0.05

failed treatment. No relapse cases were detected. Severe side effects (hypokalemia, depression, psychosis, seizure, nephrotoxicity or hepatoxicity) were observed in 35% of the cases but not associated with poor treatment outcome. 61% (19/31) of the defaulters stopped treatment during the intensive phase. From the beginning throughout treatment, defaulters had a higher percentage of missed treatment days than cured patients. Only 36% of the 25 MDR-TB patients with poor adherence (>20% of treatment days missed) were cured. The table presents other risk factors for poor treatment outcome. In a multivariate logistic regression model, high percentage of treatment days missed, body weight at treatment start below 47 kg (median weight), and resistance to a 2nd-line drug were associated with default. In the FGDs, reported reasons for missed treatment and default were: adverse drug reactions, difficult access to clinic, financial burden of treatment, lack of family support and dissatisfying patient-provider relationship.

Conclusion: Missed days of treatment, especially during the first 60 days of treatment, should alert the providers that patients might default. Patients need considerable ability and willingness to endure treatment. Strengthening social and emotional support, income generating activities, psychosocial support through patient group discussions, more convenient DOT and improving access to MDR-TB treatment may prove helpful.

PS-100848-15   Programmatic management of drug-resistant tuberculosis in Indonesia: preliminary result

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Setting: PMDT pilots in Indonesia, a high burden country for TB and MDR-TB.

Objective: Indonesia aims for a uniform approach for MDR-TB management for the whole country, with only minor local operational adjustments. The uniform approach will facilitate expansion, supervision, human resource development, involvement of clinicians, drug ordering and drug-management.

Methods: Patients were consecutively enrolled after confirmation of MDR-TB status in two treatment center in two pilot sites, Persahabatan & Sutomo hospital. Confirmation of MDR-TB are done in quality assured lab with liquid methods. Standardized treatment regimens were given based on DST result and history of previous intake for other drugs that were not tested. Preliminary data, result and lesson learnt after 6 month implementation in both sites were analyzed.

Results: From May 2009 to February 2010, 241

MDR-TB suspects detected, 151 (63%) had DST result. 69 of it (46 %) confirmed as MDR-TB cases. Only 33 (49 %) out of 69 cases put on treatment. 9 of the 69 (13%) refuse treatment. Chronic cases and non-DOTS were dominant causes of MDR. Most of the MDR-TB cases came from the referral hospitals. 50% of suspects from non–DOTS group (PP's) were MDR-TB. The average time for DST were 7 weeks and average time for patients enrolled were 4.5 weeks. All side effects found were manageable.

Conclusion: Although slower than expected, the PMDT implementation achieves encouraging result. Corrective actions to speed up and scaling up the implementation will be in three essential strategies: Service improvement by improving health education methods, review SOP of diagnostic, conducting operational research on HAIN Test, implementing E TB Manager; Expand services by expanding coverage of PMDT services in existing sites and establishing new sites throughout Indonesia in-line with establishment of quality assured laboratories; and Program strengthening by developing legal-regulation in the country with the related stake holder.

PS-101045-15   Increased fluoroquinolone resistance in *Mycobacterium tuberculosis* strains from Pakistan, 2005–2009

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Introduction: Fluoroquinolones are increasingly being used for the management of both tuberculous and non-tuberculous infections in Pakistan. Recent evidence suggests high resistance in community acquired pathogens. Such resistance has been related to misuse of quinolone as well as to poor formulations. Resistance data from the region revealed increasing trend of fluoroquinolone resistance in *M. tuberculosis*. Fluoroquinolone resistance data in *M. tuberculosis* from Pakistan is limited and is urgently needed in view of large number of MDR cases.

Materials and methods: Fluoroquinolone resistance trends (2005–2009) from a referral center laboratory in Pakistan were analyzed in ≥ 2 drug-resistant *M. tuberculosis* strains (Table 1). Additionally in 2009, fluoroquinolone susceptibility was determined 1310 fully susceptible and mono-resistant *M. tuberculosis* isolates. Susceptibility against first and second line agents was tested using standard methodology. Resistance trend during the study period was assessed using χ^2 for trend analysis.

Results: A total of 4754 *M. tuberculosis* strains (2005–2009) were assessed for fluoroquinolone susceptibility. Overall resistance was 27.8% (1323/4754). Significant increasing trend ($P < 0.05$) of resistance was observed in ≥ 2 drugs resistant *M. tuberculosis* strains. In 2009 fluoroquinolone resistance was ob-

served in 3.4% of the sensitive strains and 2.8% in mono-resistant *M. tuberculosis* strains.

Conclusion: Increase in fluoroquinolone resistance from Pakistan pose a burden and increase the overall cost of management of MDR-TB cases in Pakistan. Existence of fluoroquinolone resistance in fully susceptible and mono-resistant *M. tuberculosis* strains is alarming and reflects misuse of this drug in community.

PS-101248-15   First results from a drug resistant tuberculosis program in Samegrelo region (Georgia)

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Drug resistant tuberculosis (TB) is a major public health problem in the Republic of Georgia. In 2006, multidrug resistant (MDR) TB accounted for 6.8% of new TB cases and 27.4% of previously treated TB cases. MSF started treating MDR-TB patients in the region of Samegrelo in November 2006. The handover of the program to the National TB Program started in early 2010. Here we describe patients' characteristics, culture conversion and predictors of culture conversion for patients enrolled between November 2006 and December 2009. We conducted a retrospective cohort study of newly diagnosed MDR-TB patients. We performed a univariate analysis on socio-demographic, previous treatment history, treatment adherence, side-effects and resistance-pattern indicators to detect predictors to initial culture conversion (at least two consecutive negative cultures from samples collected at least 30 days apart). Cumulative survival curves using Kaplan–Meier estimates and multivariate Cox proportional hazards model were performed. 209 patients started DRTB treatment during this period. Median age at admission was 37 years (IQR: 30–49), male:female ratio 4:1, 89.9% of patients had received previous TB treatment and 14.6% were XDR. Median time of follow up was 12.2 months (IQR: 5.7–19.6). Conversion rate was 66.3 per 100 person-year with a median time to conversion of 3.4 months (IQR: 2.3–4.8). Among 146 patients with at least 6 months follow up, 74 (50.7%) converted. Univariate analysis identified age, baseline resistance to ofloxacin, and low Body Mass Index at admission as predictors of culture conversion. In the multivariable model, only resistant to ofloxacin (HR 0.15; CI95% 0.05–0.48) and BMI (HR 1.06; CI95% 1.02–1.11) remained significant. In this high DRTB prevalence, success in culture conversion could be achieved in 50% of MDR patients within 3 months of starting treatment. As previously suggested, resistance to ofloxacin is a key factor in achieving culture conversion.

PS-101365-15   Adverse events in patients hospitalized with multidrug-resistant tuberculosis: a prospective cohort

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Background and aim: About 10 000 cases of multidrug-resistant tuberculosis (MDR-TB) cases are diagnosed annually in South Africa. There is little prospective data on adverse events of MDR-TB treatment in HIV-infected and HIV-uninfected individuals.
Methods: Prospective cohort study conducted at Sizwe Tropical Disease Hospital, the MDR-TB referral Hospital for the South African Gauteng province.
Results: Between August 09 and Feb 10, data was collected on 38 patients hospitalized for MDR-TB treatment. 60% ($n = 23$) were female, mean age of 33.7 years (standard deviation 8.26). Seven (18%) cases had spent time in prison, 4 (10%) were health care workers, and 1 mine worker. The majority (31, 82%) were HIV infected of which 25 (80.6%) were on antiretroviral treatment (ART) on admission to the MDR hospital. Primary MDR occurred in 15 (37.5%) cases, all in HIV positive individuals. In the 114 months of follow up (median follow up 3.0 months), there were 2 deaths (5.2%), both among HIV-infected patients. 125 adverse events were observed of which 58% ($n = 73$) occurred in the first month of treatment, 23% ($n = 29$) occurred in the second month, and 18.4% ($n = 23$) in the third month. 23 events (18.4%) were neurological, 23 events (18.4%) gastroenterological , 13 (13%) dermatological and 17 (10.4%) were infectious. Adverse are more likely to occur in HIV infected compared to HIV-uninfected individuals (87.2% vs. 13.6 %, $P = < 0.001$). 23 adverse events were attributed to MDR-TB drugs and 13 attributed to the ART. The rest of the AE were not drug related. Risk of severe adverse events was higher in HIV-infected patients (RR 1.5, 95%CI 0.51 to 4.70).
Conclusion: In our setting, one in four hospitalized MDR-TB cases occurred in either ex-prisoner or health care worker. High occurrences of adverse events were observed especially in the first month and among HIV-infected patients. HIV co-infected patients also tended to be at higher risk of severe adverse events.
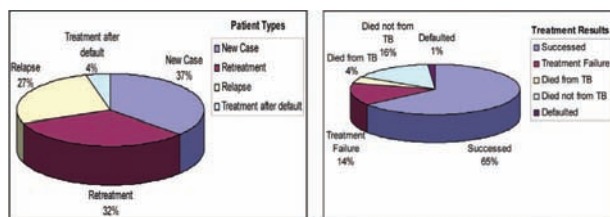
PS-100441-15   Initial outcome of MDR-TB treatment in central Taiwan

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Background: Around 1% of the newly reported TB cases in Taiwan are MDR-TB. The Taiwan CDC provides a budget of NT$400 millions each year on the DOTs-plus program. They allow NT$800 000 per patient annually for the anti-TB treatment. Changhua Hospital conducted hospitals surrounding the central Taiwan and supervised their DOTs-plus work. This report reviewed our initial outcome of the DOTs-plus program and aimed to establish a professional medical system of treating MDR-TB and control prevalence of MDR-TB.
Methods: Any subjects from May 2007 to January 2010 resistant to isoniazid and rifampin as confirmed by the Reference Laboratory of Mycobacteriology were included in the study. Medications for all subjects were delivered by our DOTs-plus car team workers in twice daily door to door basis to ensure the compliance, and any adverse effects were monitored and reported back to the hospital immediately. If the subjects were difficult to be reached, 3G visual mobile phones were provided to the workers to ensure drug intake by the subjects, but no more than 4 days per month. This program was managed by a supervisor who randomly would visit the subjects to find out feedback of the DOTs-plus program and the health workers. In order to increase the patient compliance, a financial support of NT$6000 monthly was provided for those who needed.
Results: 145 MDR-TB subjects in the program with 71 subjects who had completed the two year treatment —32% were retreatment, 27% were relapsed, 4% were defaulted and 37% were new cases. Forty-six subjects (65%) were successfully treated, 10 (14%) failed, 3 (4%) died from TB, 11 (16%) died from non-TB and 1 (1%) defaulted. This indicated the implement of the intensive follow-up and monitoring improved the patients' compliance and increased the cure rate and reduced the default rate.

Conclusions: The initial outcome of MDR-TB DOS-plus program showed an impressive result especially in the defaulted rate that only 1 patient was defaulted.

PS-100565-15   Preliminary results of the treatment of first 100 MDR-TB patients

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Aim: All diagnosed MDR-TB patients are enrolled in Drug resistant treatment and infection control measures, tailored DR TB treatment and medical management of co-morbidities according to WHO standards are implemented.
Methods: Medical record of first one hundred patients enrolled in the program have been analyzed and data's released prisoners under treatment were collected from civilian TB registers in the frame of the tripartite agreement between Ministry of Justice, Ministry of Health and ICRC.
Results: Since April 2007 to September 2008, 100 patients have been enrolled to the individualised MDR Treatment project. Interim results of the project show that 59 patients have been cured, 10 patients died, 7 patients defaulted treatment, 4 patient failed, 3 patients were transferred to civilian sector, and the rest, 17 patients, are still on treatment. 75% of patients converted within first 12 months of treatment with an average time of conversion being 3–4 months from the beginning of treatment.

Out of 100 patients:

Cured	Died	Defaulted	Failed	Transferred out	Still on treatment
59	10	7	4	3	17

Last patients will finish their treatment in September 2010, and by than we expect results to become final.
Conclusion: Results with 59% of cure rate can be interpreted as successful experience and it will contribute to build the capacity of the Azerbaijani authorities to plan and implement individualized Drug Resistant treatment program for all DR TB patients from the entire penitentiary system.

PS-101162-15   MDR-TB treatment success rates for 7 years of program implementation in the civilian sector, Tomsk, Russia

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Background: The MDR-TB project in Tomsk, Siberia was the first DOTS Plus project piloted in Russia. The Tomsk project was launched in September 2000 in the prison sector and extended to the civilian sector in January 2001. The initial treatment success rate of the first cohort of patients (134) was relatively good—72.2%. However, as the project expanded to

cover more DR-TB patients, especially in rural areas, the treatment success rate began decreasing (to 54.3% in 2004), and default and failure rates rose.

Methods: Between 2000 and 2004, the Tomsk DR-TB project employed advanced clinical monitoring of patients, aggressive management of side effects, provision of monthly food packages, improvement of rural DOT and organization of MDR-TB treatment at home in the Tomsk city. Beginning 2005, in addition to the existing activities, patients were provided with daily food packages, hygiene sets and reimbursed for local transportation based on the support from the GFATM. Since 2006, patients with substance abuse were offered treatment through an anti-alcohol subprogram and the Sputnik accompagnateur program was launched for high-risk patients.

Results: 1099 patients were enrolled in the civilian sector DR-TB program between 2001 and 2009 (out of total 1580 enrolled in both civilian and prison sectors). As of November 30, 2009, treatment outcomes were registered for 939 patients in the civilian sector. Treatment success rate increased U-shaped from 54.3% for 2004 cohort to 72.7% for 2007 cohort.

Conclusion: Good treatment success rate of MDR-TB treatment are feasible to achieve if a program employs appropriate activities to improve patients' adherence to treatment.

PS-100653-15   Establishment of the first state-of-the-art DR-TB ward linked to a BSL-3 TB laboratory in Nigeria

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Background: Nigeria ranks 4th among 22 high burden TB countries. WHO estimates that 1.9% of new TB cases and 9.3% of re-treatment cases in Nigeria are MDR-TB. This translate to an estimated 2095 MDR-TB cases. While two BSL-3 TB laboratories have been recently established in Nigeria, treatment centres for MDR/XDR-TB were not available. We describe the establishment of the first dedicated state-of-the-art MDR/XDR-TB treatment centre linked to the BSL-3 TB laboratory in Cross River State, Nigeria.

Interventions: Site selection through federal and state government; local capacity building in design and renovation of DR-TB ward; renovation; staffing and training; development of infection control systems; establishment of planned preventive maintenance (PPM) system; link with BSL-3 TB lab and network of peripheral TB-dots facilities; M&E system.

Results: An old TB ward of the infectious disease hospital in Calabar hosting the BSL-3 TB lab was selected as renovation site. A Nigerian team of clinicians, architects and infection control specialists was trained in South Africa on hospital and community management of DR-TB. The renovation for the 20-bed ward included recreational and security aspects for long-term hospitalization. The first national curriculum for DR-TB management was developed and 31 service providers trained. A hospital committee monitors best practice of an integrated infection prevention and control plan. Together with state and facility engineers, GHAIN introduced a PPM system for infrastructure and equipments of the ward and lab. A sample transport system links 96 peripheral TB DOTS facilities and a community TB pilot district with the reference centre. An electronic medical record system, LAMIS, developed by FHI/GHAIN, links all patient and lab data and provides summary statistics for the national TB control programme.

Conclusion: Core infrastructure and systems are now in place to address the DR-TB epidemic in Nigeria.

PS-100260-15   Quality of services for management of MDR-TB patients in clinics of Nepal: a qualitative study

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Aim: The Nepal National Tuberculosis Control Programme started DOTS PLUS PILOT project from 2005 using 24 months treatment regimen. There are many factors or barriers that may affect adherence to the long treatment regimen. Lack of essential resources for diagnosis and treatment and unskilled health man power are associated with poor treatment adherence in long term treatment like. Perceptions and attitudes of MDR-TB patients on facilities available at DOTS-PLUS clinics in Nepal was ascertained through this study.

Methods: The study was conducted as an institution based qualitative study, using a convenience sampling technique. Data was collected from 50 current MDR-TB patients by trained field health workers using semi structured interviewer administered questionnaire in five regions of Nepal.

Results: The study revealed that, the DOTS Centres in Eastern, Mid and Far Western regions in Nepal had most of the essential resources required for the provision of care to MDR-TB patients. In contrast DOTS Plus centres in Western and Central regions were lacking certain essential facilities such as drinking water, maintenance of cleanliness and competence of health workers especially giving intra muscular injections.

Conclusion: Special emphasis should be laid by the National Programme in improving aspects of care in Western and Central regions in Nepal. This should be accompanied by provision of infrastructure facilities in the DOTS PLUS clinics such as personal protection equipments, adequate space and ventilation, facilities for hand washing etc.

PS-100262-15   Barriers to directly observed treatment for MDR-TB patients in Nepal: a qualitative study

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Aim: Nepal's National Tuberculosis Control Programme started DOTS PLUS PILOT project using 24 months treatment regimen in 2005. To prevent XDR-TB, it is important to adhere to this long duration of drug regimen. There are many factors or barriers that may affect adherence to the long treatment regimen. The aim was to find out the barriers for adherence to MDR-TB treatment under DOTS-Plus programme.
Methods: An institution based qualitative study, using a convenience sampling technique. Data was collected from 50 current MDR-TB patients by trained field health workers using semi structured interviewer administered questionnaire in five regions of Nepal. Twenty five focus group discussions (FGD) were also conducted with MDR-TB patients, cured MDR-TB patients, DOTS Committee Members, health workers and close relatives of MDR-TB patients to supplement the findings.
Results: Majority of patients had a previous history of irregular TB treatment. Forty out of fifty patients (80%) were living in either rented houses or hostels (in Mid Western Region). Majority of participants (98%) were highly satisfied with facilities and services provided by DOTS-Plus clinics. Lack of money to go to health facility daily for treatment for 24 months and side effects of medicine were reported as major barriers to adhere to DOTS Plus treatment
Conclusion: DOTS-Plus programme in Nepal is doing commendable service to MDR-TB patients. Financial constraint was the major barrier for these patients. To sustain DOTS-Plus programme, Government of Nepal and other organizations may seek additional resources to provide social support to these patients.

PS-100279-15   MDR and DRTB treatment strategies: experience from the first program in Kenya

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Background: Kenya is one of the highest TB burden countries with an incidence of 353/100 000 in 2007. The MDR-TB prevalence is estimated at 1.9% of new TB cases.
Intervention: In 2006, MSF started the first DR-TB program in the country in two sites. Here is described the experience of implementing two different DRTB models of care.
Results: Drug susceptibility test (DST) was performed in category I patients still smear positive after 3 months

of treatment, in category II patients prior to start treatment, and in failure cases. Treatment regimens were individualized.

Mathare program was clinic-based and patients came daily to the clinic to receive directly observed treatment (DOT). This strategy allowed patients to continue their income generating activities and to take care of their families. A day-care unit was created with specific space allocated and a multi-disciplinary team providing medical, psychological and social care. In Homa Bay patients were hospitalized until sputum conversion then treatment was ambulatory. Patients from the periphery were relocated in town. In 2008, a community based model was set up for the continuation phase of treatment. A DOT supporter ensured the daily supervision of the treatment at home. In 2010 the intensive phase will be decentralized. From May 06 to February 10, culture was done for 442 patients, 107 (24.2%) were positive and a DST was performed on them. Resistance to rifampicin and isoniazide was found in 44 (9.9%) patients, resistance to at least one first line drug in 16 (3.6%). Additionally six patients were diagnosed with MDR-TB while carrying out a DST survey in Homa Bay. In total, 53 MDR-TB patients have been started on treatment in the program: 15 are cured, 5 died, 3 defaulted, and 30 are still on treatment.
Conclusion: MDR detection and treatment strategies should be adapted to the context of the program and can coexist if necessary. The first DRTB program in Kenya has shown encouraging results.

PS-101193-15   Multidrug-resistant tuberculosis in the Pacific

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Background and challenges to implementation: The Pacific region is made up of 22 island countries and territories with diverse populations, cultures and economies. Multidrug-resistant tuberculosis (MDR-TB), defined as TB resistant to at least isoniazid and rifampicin, is posing a substantial threat to TB control in the Pacific Island countries and territories (PICTs) due to its complex diagnostic and treatment challenges. If available data indicate low level of drug resistance in the southern Pacific, the resistance levels are already alarmingly high in some PICTs, especially the Micronesian.
Intervention: A joint effort of the Centers for Disease Control and Prevention, the Secretariat of the Pacific Community and the World Health Organization helped the Federated States of Micronesia and the Marshall Islands to conduct an investigation of MDR-TB outbreaks, to manage cases effectively and to strengthen the TB programmes. Measures taken included procurement of second-line drugs; hiring of outreach workers to ensure directly observed treat-

ment, construction of an isolation ward, holding training workshops for the newly appointed staff and ongoing technical support and medical consultation with MDR-TB experts.

Results and lessons learned: Major constrains have been timely provision of second-line drugs, long-term management of patients on isolation and laboratory services support. The geographic spread and isolation of the islands combined with high mobility of TB patients and their contacts have been additional challenges.

Conclusions and key recommendations: A coordinated response involving multiple agencies has proven effective however there is a need to support the development of a framework of response to drug-resistant TB in the Pacific that will link the critical aspects of case management of MDR-TB, i.e., laboratory services, technical/clinical support for case management, and the timely provision of second-line drugs.

MOLECULAR EPIDEMIOLOGY OF TUBERCULOSIS

PS-100053-15   Genotyping of *Mycobacterium tuberculosis* isolates in Dohuk City, Iraq using MIRU-VNTR

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Background: Tuberculosis (TB) is the second most common cause of death worldwide after human immunodeficiency virus (HIV) resulting from a single infectious agent. One measure for effective control of TB is good understanding of TB epidemiology to understand transmission pattern of the disease. MIRU-VNTR typing demonstrated a highly reproducible and fast genotyping system of *M. tuberculosis* clinical isolates. Here, we studied *M. tuberculosis* strains homogeneity and the transmission pattern among TB patients; to our knowledge, this is the first report about the molecular basis of strains prevailing in Iraq.

Methods: The 12 standard MIRU-VNTR loci were used to genotype *M. tuberculosis* isolates from Duhok, Iraq. The www.miru-vntrplus.org website was used for strain identification and phylogentic analyses among the isolates.

Results: A total of 51 MIRU profile were obtained for the 51 samples tested. All specimens showed amplification products of all MIRU-VNTR loci, and all of them showed differences in at least one locus. The identification by similarity showed that 18 (34.3%) of the isolates were genotyped and the rest 33 (64.7%) were not. Overall, the distribution of identified lineages was unknown (64.71%), S (13.73%), LAM (9.80%), Delhi/CAS (3.92%), Bovis (3.92%), Haarlem (1.96%), and Ural (1.96%).

Conclusions: Majority of strains isolated from Duhok, Iraq, were not classified. Among the classified strains the majority belonged to modern *M. tuberculosis* genotype. Our results suggest that different lineages of *M. tuberculosis* were circulating in this city. Therefore, the reactivation of latent infections would be responsible for the endemic situation of TB. Furthermore, we conclude that a big circle of TB transmission might be missed, which means effective control measure has not been achieved in Iraq.

PS-100156-15   Study of GC content in regulatory gene whiB7 from Belarusian resistant isolates of *M. tuberculosis*

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Regulatory gene of whiB7 transcription determines drug resistance in *Mycobacterium tuberculosis*. Increases in WhiB7 protein activity, induces transcription of resistance genes leading to intrinsic multidrug resistance. Thirty three clinical isolates of *Mycobacterium tuberculosis* were done for sequencing of gene whiB7. We found that this gene is highly conservative and there is not any mutation in entire promoter (429 bp) and structural gene (279 bp) of whiB7 in resistance forms (MDR, XDR) and susceptible clinical isolates of *M. tuberculosis*. GC-content in third codon positions (3GC) of the gene coding for whiB7 is lower than the average 3GC level in 3965 ORFs from completely sequenced *Mycobacterium tuberculosis* H37Rv genome (66.67% versus 78.81 ± 0.17%). The usage of Arg2 (AGA/G) codons in whiB7 gene is much higher than its average level in *Mycobacterium tuberculosis* H37Rv ORFs (4.3% versus 0.53 ± 0.02%), moreover it is higher than in whiB7 homologues from other actinomycetales. The last feature is caused by the duplication of relatively GC-poor sequence (CCCCAGACAGA) in the region coding for the N-terminal of WhiB7 protein. This duplication happened before the divergence of *Mycobacterium tuberculosis* and *Mycobacterium bovis*. *Mycobacterium marinum* and *Mycobacterium leprae* contain unduplicated homologous sequence in gene coding for whiB7, while *Mycobacterium smegmatis* lacks it. Gene coding for whiB7 is expressed only as a response to the stress conditions, these conditions in turn may influence the rates of nucleotide mutations mostly in the expressed genes leading to the relative decrease of 3GC in whiB7 coding region.

PS-101504-15   Molecular genotyping of *M. tuberculosis* from patients with cavitary, noncavitary and extrapulmonary TB

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Background: Based on the hypothesis that genetic variability of *Mycobacterium tuberculosis* could influence virulence and immunopathology we analysed the genetic profiles of different *M. tuberculosis* strains in order to detect relatedness between genetic diversity and disease severity.

Methods: We conducted a retrospective molecular study in Vitória, ES, Brazil based on culture-positive TB strain (2003 to 2006, $n = 245$) from patients with pulmonary (minimal non-cavitary disease, advanced non-cavitary disease and advanced cavitary disease) and extrapulmonary TB using IS*6110*-RFLP and Spoligotyping methodologies.

Results: Among all *M. tuberculosis* strains studied, 197 were pulmonary strains and 48 were extrapulmonary. Our results demonstrated that 26.94% (66) of the strains were grouped in 18 clusters based on IS*6110*-RFLP and the analysis of these clusters showed no association with disease severity. Each strain was characterized by spoligotyping and the pattern compared with the national and worldwide SpolDB4.0 databases. LAM9 was the most common family detected (12.24%) followed by T1 (6.12%), LAM1 and U (5.71%). In addition, 97 strains (39.6%) were found in SpolDB4.0 as non described. There were no association between IS610-RFLP clusters and spoligotyping families.

Conclusion: Our data showed that LAM9 was the most frequent among the strains studied corroborating findings that this family is the most frequent in Brazil. There were no statistical differences that could show association among the variables analysed related to disease severity.

PS-100707-15   Phenotype, genotype and relationship with *M. tuberculosis* drug resistance in Viet Nam

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Aim: Phenotype, genotype are the important biomarkers to monitor epidemiological tuberculosis. Drug-resistant TB bacteria related to phenotype and genotype should be more than interested in order to monitor multidrug-resistant tuberculosis.

Methods: Our research were done base on a national representative sample. All *M. tuberculosis* strains isolated from TB prevalence survey in Viet Nam in 2007 were included in the study. Standard biochemical as-

says were performed for phenotyping. Spoligotyping was performed with a commercial kit. RFLP analyses were performed follow standard SOPs. Drug susceptibility test were done base on conventional proportion method. The relations between phenotype, genotype and drug resistance were analyzed.

Results: 232 *M. tuberculosis* strains isolated from 7648 TB suspects in 70 clusters in the whole country. Two phenotypes were detected: Asian variant (51.3%) and classical variant (48.7%). 16 sopligo type were determined, including two large groups of Beijing (36.5%) and East Africa Indian-EAI (39.1%). 65.5% of classical variant is Beijing genotype. 77.8% of Asian variant strains were identified as EAI genotype. Beijing strains have closely relationship with drug resistance, particularly MDR (any drug: 41.7 %, MDR: 8.3%) comparing with the EAI strains (any drug: 17%, MDR: 2%) ($P < 0.001$). The difference much bigger when comparing Beijing genotype among classical strains with EAI genotype among Asian strains: MDR rate was 9.1% compared with 1.3% ($P < 0.001$). RFLP results still being analyzed and up date soon.

Conclusion: In Viet Nam, phenotypes of *Mycobacterium tuberculosis* circulating are Asian and classical variant. Beijing and EAI are most popular genotypes circulating. There are very strict relations between genotype, phenotype and MDR: the classical strains with Beijing genotype and MDR; Asian strains with EAI genotype and TB drug susceptible.

PS-100669-15   Spoligotyping of serial *M. tuberculosis* isolates from MDR-TB patients in Russia

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Background: As part of the Preserving Effective Tuberculosis Treatment Study (PETTS) we collected serial *M. tuberculosis* cultures from the sputum of patients with multidrug-resistant TB (MDR-TB) (resistant to both isoniazid and rifampicin) who were starting second-line drug (SLD) treatment from 01/2007 to 12/2008.

Methods: We spoligotyped cultures using standard methods and compared spoligotypes of serial cultures from the same patients to determine if they were identical. We performed real time PCR with primers for IS*6110* to ensure all positive mycobacterial cultures were *M. tuberculosis* complex.

Results: A total of 416 cultures were obtained from 127 patients. One was PCR-negative, identified as *M. fortuitum* with the GenoTypeAS/CM test (HAIN LifeScience, Germany). Spoligotyping was performed

on 343 serial isolates from 77 patients. Of these, 278 (81%) isolates from 67 (87%) patients had the same spoligotype throughout treatment. Of these 278, 244 (88%) belonged to Bejing family (58/67 [87%] patients), 11 (4%) to Haarlem3 (2 [3%] patients), 14 (5%) to LAM9 (5 [7%] patients), and 9 (3%) to T4 (2 [3%] patients). Spoligotypes changed during treatment in 10/77 (13%) patients (65 isolates). In 5/10 patients, 1 isolate in the series was completely different than the others in the series. In 4/10, loss of spacers in direct repeat region was detected. In 2 patients, an isolate appeared to gain a spacer region.

Conclusion: The majority of *M. tuberculosis* strains belonged to Beijing spoligotype. In 10/77 patients, the spoligotype of at least 1 isolate differed from other isolates in the series. This may represent contamination in the lab, mixed infections with different strains in the patient, or changes in staining intensity of bands after electrophoresis. This specific reason could not be determined by spoligotyping. More discriminating genotyping methods for assessing clonality (24-Locus MIRU-VNTR) will be implemented.

PS-100075-15   Characteristics of MIRU-VNTR genotyping in sub lineages of Beijing strain *Mycobacterium tuberculosis*

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Background: Beijing (BJ) strain *Mycobacterium tuberculosis* is widely distributed around the world and associated with higher drug resistance rate in some areas. The composition of sublineages of BJ strain and their characteristics in MIRU-VNTR genotyping remained to be elucidated.

Design/methods: Clinical isolates were collected from newly diagnosed culture-proven tuberculosis patients at six hospitals in Taiwan. All isolates were genotyped by standard spoligotyping and 12-loci MIRU-VNTR methods. Sublineages of BJ strain were divided into ancestral, modern, and W-branch according to IS*6110* insertion in NTF region. The characteristics of MIRU-VNTR genotyping in sublineages of BJ strain and their discriminative power were analyzed.

Results: A total of 401 clinical isolates, included 174 BJ strain and 227 non-BJ strain, were collected for analysis from Jan. 2007 to Dec. 2009. Among BJ strain isolates, 37 (21.3%) were ancestral sublineage, 54 (35.9%) were modern sublineage, and 73 (42%) were W-branch sublineage. In MIRU-VNTR genotyping, locus 4, 23, and 24 have low allelic diversity

Table Twelve loci MIRU-VNTR genotyping of clustered Beijing strains and their composition of Beijing strain sublineages

Clus-ters	Spoligo-typing	2	4	10	16	20	23	24	26	27	31	39	40	Total no. of strains	Sub-lineages of Beijing strain
1	Beijing	2	2	2	3	2	2	5	1	6	3	5	2	3	W-branch
2	Beijing	2	2	3	3	3	2	5	1	8	4	4	2	3	W-branch
3	Beijing	2	2	3	3	3	2	5	1	7	3	7	1	2	Modern
4	Beijing	2	2	2	2	3	2	5	1	7	3	4	3	2	Modern
5	Beijing	2	2	4	2	3	2	5	1	8	3	4	6	2	Modern
6	Beijing	2	2	2	4	2	5	5	1	6	3	4	1	2	Modern
7	Beijing	2	2	1	3	2	2	5	1	8	3	4	3	2	W-branch
8	Beijing	2	2	3	5	3	2	5	1	8	4	6	3	2	W-branch
9	Beijing	2	2	2	2	2	2	5	1	6	3	4	2	2	W-branch
10	Beijing	2	2	1	2	2	2	5	1	8	3	4	3	1	Ancient
														1	W-branch
11	Beijing	2	2	1	1	2	2	5	1	8	3	4	3	1	Ancient
														1	W-branch
12	Beijing	2	2	4	3	3	2	5	1	7	3	4	2	1	Modern
														1	W-branch
13	Beijing	2	2	3	2	1	2	5	1	7	3	4	2	1	Modern
														1	W-branch
14	Beijing	2	2	3	4	2	1	5	2	6	3	6	3	1	Ancient
														1	Modern

Sublineages of Beijing strain are divided according to IS6110 insertion in NTF region. MRU-VNTR = Mycobacterial Interspersed Repetitive Unit Variable Number Tandem Repeat

(<0.3) in BJ strain but have moderate to high allelic diversity (≥0.6) in non-BJ strain. The clustering rates in ancestral, modern and W-branch sublineages were 0%, 6.3% and 10.9% respectively. The distribution of copy numbers of 12-loci MIRU-VNTR was comparable between sublineages of BJ strains. Combined MIRU-VNTR genotyping and spoligotyping, 14 clusters (19 isolates) were identified in BJ strain. Among these isolates, five clusters (10 isolates) are composed of different sublineages of BJ strain and were considered as false clusters.

Conclusion and recommendations: W-branch sublineage was the dominant sublineage of BJ strain in Taiwan and was associated with higher clustering rate. Subtyping of Beijing strain could differentiate strains with identical 12 loci MIRU-VRTR genotyping, which made this method a useful tool in epidemiologic analysis.

PS-100436-15   Molecular epidemiology of *Mycobacterium tuberculosis* in Kiribati

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Aim: Tuberculosis (TB) remains an important infectious disease globally and in the Pacific nation, Kiribati, where case notification is 423/100 000 (2007), but risk factors for transmission are poorly understood. We investigated molecular and epidemiological factors associated with the ongoing TB epidemic in Kiribati.
Methods: Sputum and structured questionnaires were collected from patients presenting with TB symptoms at the central hospital in Kiribati. Sputum was cultured, isolates genotyped using two methods, (MIRU-VNTR and spoligotyping) and drug susceptibility testing performed.
Results: 163 patients were recruited from 13 Kiribati atolls (55% female) and 74 samples were culture positive. High residential density (median number of people/house = 9) was common in those tested. Genotype analysis revealed the majority of isolates belong to major clades of *M. tuberculosis* (Beijing 47%; LAM 16%; S 12%; Other 24%), with 68 distinct patterns and 2 clusters of 2 and 5 solates each. Beijing genotype was more common in house workers (62%) and patients from the largest atoll (79%), but was found across all 14 villages. Two isolates were found to have mono-resistance to Streptomycin (non Beijing). No other drug resistance was detected. Only nine patients were tested for HIV, none positive.
Conclusion: This is the first report of prevailing TB strains in Kiribati and suggests a diverse TB epidemic exists. Although drug resistance is limited, the prominence of the Beijing genotype in Kiribati is cause for concern and may be responsible in part for the emerging TB epidemic. Although clustering is limited in this small sample, the age distribution of cases suggests active transmission, with high residential density a likely contributor. This suggests that a targeted preventative transmission approach should be adopted in Kiribati, utilising active case detection, contact tracing and public education encouraging early diagnosis to reduce the future impact of TB.

PS-100471-15   Genotypic diversity of *M. tuberculosis* isolates in North Delhi, India

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Background: The use of repetitive elements has made molecular typing of *M. tuberculosis* very convenient and has facilitated studies on molecular epidemiology of *M. tuberculosis*. Very few studies in India have reported use of MIRU-VNTR typing and spoligotyping of *M. tuberculosis* isolates.
Design: We attempted to analyze the genetic diversity of *M. tuberculosis* isolates ($n = 101$), obtained from 134 patients of pulmonary tuberculosis in North Delhi region, India, by spoligotyping, MIRU-VNTR typing and IS*6110* RFLP typing.
Results: Spoligotyping subdivided the strains into 49 types, including 14 clusters and 35 unique types. The most frequent spoligotype was SIT26, followed by SIT11, representing 20.8% and 10.9% respectively, of all strains in the study. IS*6110* RFLP typing was carried out for 80 of the 101 isolates studied, including all the isolates found to be clustered by spoligotyping. RFLP typing could genotype 62 *M. tuberculosis* strains with high copy number of IS*6110* bands into the same number of unique types. Eighteen isolates had low copy number of IS*6110* bands and could not be typed by RFLP. An 11 locus MIRU-VNTR typing was applied to all 101 isolates. MIRU-VNTR could differentiate all the isolates into unique types. MIRU locus 31 was found to be most discriminatory with an allelic diversity of 0.76. The Discriminatory power (Hunter-Gaston Index) of spoligotyping, IS*6110* typing and MIRU-VNTR typing was found to be 0.94, 0.99 and 1 respectively.
Conclusion: In conclusion, the 11 loci MIRU-VNTR typing method was found to be most discriminatory for the *M. tuberculosis* strains in North Delhi and emphasized the rich diversity of *M. tuberclosis* isolates in this region. An optimum set of MIRU loci required as the first-line typing tool, may vary between countries. Further studies would be required in India to test these loci.

PS-100476-15   Significance of molecular epidemiology and GIS in modulating MDR-TB transmission in endemic Mumbai, India

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Transmission of multidrug resistant tuberculosis (MDR-TB) is a major public health concern in TB control in Mumbai, India. High levels of MDR-TB

have been reported from Mumbai (D'souza et al. BMC Pub. Health 2009) which has 54% of its population residing in vulnerable environments. This necessitates detailed information and novel methods of intervention. A study by us involved longitudinal sampling of new pulmonary TB patients from 4 municipal wards of Mumbai, with a population of 3 million accessing treatment at 52 health posts (HP). Cultured isolates from patients at intake and 5th month follow up were subjected to drug susceptibility testing (genotypic and phenotypic) and strain typing (spoligotyping and 12 Loci MIRU-VNTR). We found that 32% of patients sensitive/mono resistant at onset, demonstrated MDR-TB at 5th month. Only 66% of the patients retained their strain type. Additionally 6/52 HPs demonstrated an increase in strain clustering (7–17%) amongst the patients at follow-up, as compared to at intake. Cumulatively this suggests that among other locales, HPs may be hubs of MDR-TB transmission/cross-infection due to patient conglomeration at these centers for long durations. The transmission risk of MDR-TB at the ill equipped HPs underscores the need for infection control which can have a substantial impact in such endemic settings. An innovative way for guiding infection control would be the assessment of standardized incidence ratio of TB based on longitudinal global positioning of patients and the HPs along with data such as number of patients, failures, relapses and degree of strain clustering. Assessing spatio-temporal changes using GIS the relative risk of contracting MDR-TB at a HP can be calculated. The impact of infection control can be assessed by clinical examination of health staff and measuring their levels of exposure. The patterns of analysis contributing to improved TB control will be presented as a prototype for implementation in endemic settings such as Mumbai.

PS-100881-15   Spatial analysis of tuberculosis epidemiological and molecular data in Vitória-ES, BRAZIL

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Introduction: Molecular typing of *M. tuberculosis* isolates is a powerful tool for studying the dynamics of TB transmission while geoprocessing allows concomitant analysis of clinical and epidemiological data on spatial basis.
Objective: To study the spatial relation between tuberculosis epidemiological and molecular data in Vitória-ES, Brazil.
Methods: Patients notified from January 2003 to December 2007 with available isolates were selected for the study. Molecular data (IS*6110*-RFLP analysis) were associated to clinical and epidemiological data (using STATA and TerraView softwares) and risk factors were sought for infection with an RFLP cluster pattern strain, inferred to represent recent transmission.
Results: Of the 410 isolates analyzed, 170 (41.4%) were grouped into 54 distinct clusters. By bivariate analysis, sex, age, race, HIV infection, and TB clinical form showed no statistically significant difference for patients belonging to cluster patterns and those that had unique patterns. The frequency of smear positive TB patients belonging to cluster patterns was significantly greater than that observed for those that had unique patterns (76.9% vs. 67.1%, respectively; OR 1.58, $P = 0.03$). Fifty percent of clustered patients live in 3 of the 7 sections in which the city is divided and 49% of clusters belonged to only three RFLP cluster 'families'.
Conclusion: These results suggesting that incidence of TB in Vitória may be influenced by a small subset of actively circulating strains. Knowledge regarding recent TB transmission is important to improve TB control programs in order to substantially reduce the incidence of this disease.

PS-101475-15   The population structure of *Mycobacterium tuberculosis* in various countries

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Background: Studying changes in the population structure of *M. tuberculosis* is important to understand the adaptation of this infectious agent to control measures. Comparing isolates of older patients (endogenous re-activations of remote infections) with those of young patients (recent infections) is especially relevant because the isolates from the older patients in general reflect the bacterial make-up in the era before the introduction of anti-tuberculosis drugs and BCG vaccination.
Methods: We have investigated possible associations of *M. tuberculosis* genotypes with patients' age and BCG vaccination status in Nepal ($n = 82$), Nigeria ($n = 212$) and Yemen ($n = 417$). The isolates from these countries were obtained within the framework of a multi-country randomized controlled trial. To investigate whether particular *M. tuberculosis* genotypes are associated with the spread of MDR-TB in Rwanda a case-control study was performed ($n = 90$). This study included all the MDR-TB cases and randomly chosen controls from the national drug resis-

tance survey conducted in 2005. All isolates were subjected to spoligotyping to determine their genotype.

Results: The Beijing and CAS genotypes were predominant in Nepal, representing 22% and 40% of the isolates, respectively. The CAS genotype was more frequent among patients younger than 30 years compared to older patients ($P = 0.035$). Furthermore, CAS genotype strains were more frequent among BCG vaccinated than among non-vaccinated individuals; 46% versus 37%. The LAM genotype predominated in Nigeria (67%), followed by the Africa genotype (14%). Little differences were observed among the distribution of *M. tuberculosis* genotypes by the age or by BCG vaccination status of the patients. The T (52%) and CAS (27%) genotypes were predominant in Yemen. In Rwanda nearly all (93%) *M. tuberculosis* isolates belonged to the T-family.

Conclusion: The population structure of *M. tuberculosis* varied significantly in Nepal, Nigeria, Yemen and Rwanda.

PS-100227-15 Are Beijing/W strains an emerging public health threat in a major immigrant-receiving country?

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Background: Tuberculosis (TB) resulting from Beijing/W strains is globally concerning due to associations with outbreaks, antituberculosis drug resistance, and treatment failure and relapse. Being a major immigrant-receiving country, this study aimed to determine if Beijing/W strains represent an emerging public health threat in Canada.

Design/methods: This population-based cohort study investigated the *M. tuberculosis* isolates from culture positive TB cases diagnosed in the province of Alberta, Canada between 1990 and mid-2007. Isolates were Beijing/W genotyped with PCR screening for genomic deletion RD105 and DNA fingerprinted with IS*6110* RFLP. Demographic and clinical data were obtained from the provincial TB Registry. Logistic regression was used for analyses.

Results: 356 (19%) of 1897 isolates were Beijing/W. Of Beijing/W strains, 299 (84%) were immigrants from the Western Pacific, 36 (10%) were immigrants from elsewhere, and 21 (6%) were Canadian-born. First Nations, a Canadian-born population burdened with TB, only had 5 Beijing/W cases. Cases attributed to Beijing/W and non-Beijing/W strains were similar for age at diagnosis ($P = 0.07$), sex ($P = 0.35$), disease

phenotype ($P = 0.73$), sputum smear positivity ($P = 0.09$) and drug resistance [Canadian-born persons ($P = 0.63$); foreign-born persons from the Western Pacific ($P = 0.61$) and other regions ($P = 0.26$)]. A similar association between Beijing/W status and HIV status was also noted among the 905 (48%) cases with HIV test results. Beijing/W strains were less frequently associated with transmission clusters than other strains among Canadian-born persons (0.004) and equally so among foreign-born persons ($P = 0.39$).

Table Incidence of Beijing/W and non-Beijing/W strains in Alberta, 1990 to mid-2007

Sub-population	Non-Beijing/W		Beijing/W		Incidence rate ratio (95% CI)
	n (%)	IR*	n (%)	IR*	
Canadian-born First Nations	303 (19.7)	21.38	5 (1.4)	0.35	60.60 (25.68, 187.98)
Canadian-born other	344 (22.3)	0.86	16 (4.5)	0.04	21.50 (13.05, 38.04)
Foreign-born	894 (58.0)	11.16	335 (94.1)	4.18	2.67 (2.35, 3.03)
Total	1541	3.11	356	0.72	4.33 (3.85, 4.87)

*Incidence rate per 100 000 person-years.

Conclusion: Beijing/W strains pose no more or less of a public health threat than non-Beijing/W strains in Canada. It also appears that current TB control programmes can appropriately manage Beijing/W strains in a low burden country.

PS-100779-15 Genotypic analysis of *Mycobacterium tuberculosis* in homeless patients in Osaka City, Japan

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Aim: To elucidate magnitude and period of recent transmission of *Mycobacterium tuberculosis* among homeless patients in high TB endemic area in Osaka City by genotypic analysis.

Methods: In high endemic area, Airin area of Osaka City, *M. tuberculosis* isolates from homeless TB patients were obtained from 2006 to 2008. 190 isolates were analyzed on genotypic classification including variable number of tandem repeats (VNTR): JATA12 (VNTR 0424, 0960, 1955, 2074, 2163b, 2372, 2996, 3155, 3192, 3336, 4052 and 4156) and hypervariable 4 loci (VNTR 2163a, 3232, 3820 and 4120) for clustering analysis. Clusters are defined by identification of the 16-loci VNTR in this study. The results were compared with that of 274 isolates obtained from 2002 to 2004 from the same target population. They were also classified into three genetic groups according to their phylogenetic types: non-Beijing, ancient Beijing and modern-Beijing.

Results: Clustering rates were 37.9% (72/190) in 2006–2008, which did not substantially decrease from 41.6% (114/274) in 2004–2006. There were 7 patterns of strains out of 9 patterns of already known specific strains causing multiple large-scale outbreaks in the past around Japan. It account of 10% (19/190) of all isolates. Despite of the predominance of the Beijing family in Japan, the largest cluster (13 isolates) was found to belong to the non-Beijing family in the population.

Conclusion: The fact that 10% of isolates belong to strain patterns causing multiple large-scale outbreaks indicates that transmission might occur involving homeless and general public. A large cluster of less transmissible non-Beijing family among homeless TB patients implies that transmission occur in the special circumstances such as in their congregating settings.

PS-100793-15   Resistance to streptomycin determines the association between MDR-TB and the Beijing genotype

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Background: Several reports of outbreaks of multi-drug-resistant tuberculosis (MDR-TB) involving the Beijing genotype have observed that the implicated strain was also resistant to streptomycin (SMR). We explored the role of streptomycin in the association between Beijing genotype and MDR-TB in a population-based study in rural Viet Nam where streptomycin is used in standard first-line treatment regimens.

Methods: In three adjacent districts, sputum cultures and drug-susceptibility testing were done on all smear-positive TB patients registered for treatment in the period 2003–2006. Genotype was determined by spoligotyping and 15-loci VNTR fingerprinting; mixed infections and relapse cases were excluded.

Results: Available for analysis were data of 2124 of 2560 (83%) registered patients. The Beijing genotype accounted for 752 (35.4%) of infections; 85 (4.1%) had MDR-TB. Of the Beijing strains, 64 (8.5%) were MDR and 376 (50.0%) SMR. The strong association between MDR-TB and Beijing genotype (OR 6.0, 95%CI 3.6–10.0) diminished by adjustment for SMR (ORadj 2.0, 95%CI 1.1–3.5). While among patients with SMR 64 of 376 with Beijing genotype had MDR-TB (17.0%, OR 2.2, 95%CI 1.2–4.1), MDR occurred in none of 376 patients with Beijing genotype but no SMR (OR undefined, 95%CI 0–0.2; *P* for interaction 0.10).

Conclusion: The association between the Beijing genotype and MDR-TB was strongly dependent on co-existing streptomycin resistance. If SMR was present, Beijing strains had a moderately increased probability of being MDR that remains unexplained. We hypothesize that MDR-associated Beijing strains stem from a clonally expanded SMR strain that has been/is being out-selected in settings where streptomycin is routinely used in first-line treatment regimens.

PS-100943-15   Relationship between *M. tuberculosis* lineage and extrapulmonary tuberculosis

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Background: Genotyping of *Mycobacterium tuberculosis* (*M. tuberculosis*) has revealed four major lineages with differential distribution worldwide. It is not known whether different lineages are associated with different sites of infection (e.g., pulmonary vs. extrapulmonary tuberculosis [EPTB]). Understanding such differences may increase clinical consideration of EPTB, the use of the specific diagnostic tests required to diagnose EPTB, and provision of appropriate treatment to patients with EPTB. We investigated the association between *M. tuberculosis* lineage and EPTB.

Methods: All culture-confirmed cases of TB in the United States reported to the national surveillance system with routinely determined *M. tuberculosis* spoligotype-defined lineage from 2004–2008 were included. For each of the four lineages, the percentage of cases with EPTB was calculated. Controlling factors known to be associated with EPTB (sex, age, region of birth, HIV status, and race), we used logistic regression to assess the relationship between lineage and EPTB.

Results: Of 70 560 reported TB cases, 32 000 (45.4%) were culture-confirmed cases of *M. tuberculosis* that included data on lineage. Of these, 23 844 (74.5%) were pulmonary only, and 5085 (15.9%) were EPTB only. The percentages of EPTB cases differed by lineage: East Asian = 561 / 3897 (14.4%); East-African Indian = 468/1232 (38.0%); Indo-Oceanic = 1102/ 4445 (24.8%); Euro-American = 2954/19355 (15.3%) (χ^2 *P* < 0.001). Compared to East Asian lineage, odds of EPTB was greater for East-African Indian (adjusted odds ratio [AOR] = 1.6, 95% confidence interval [CI] = 1.4–1.9), Indo-Oceanic (AOR = 1.7, CI = 1.5–1.9) and Euro-American (AOR = 1.3, CI = 1.1–1.4).

Conclusions: *M. tuberculosis* lineage is associated with EPTB. In settings or populations in which EPTB-associated genotypic lineages are common, efforts to improve recognition of EPTB may be important to ensure adequate diagnosis and treatment.

PS-101160-15   Characterization of *Mycobacterium tuberculosis* strains circulating in Dakar by spoligotyping and sequencing

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Background: Tuberculosis is a highly contagious infectious disease, epidemiologic monitoring of which can be reinforced by molecular biology. The population structure of the *M. tuberculosis* complex in Senegal was last described in the 1970s using biochemical methods. We genotyped *Mycobacterium tuberculosis* isolates from patients who presented with pulmonary tuberculosis.

Methods: Genetic characterization using standard spoligotyping was applied after culture on egg based solid media on a total of 218 isolates. The strains were compared with in international spoligotyping database (SpolDB4). To speciate atypical mycobacteria, we sequenced the 16S RNA and hsp65 genes.

Results: The study population of 218 patients included 155 men (71%) and 63 women (29%), and 5 patients (2.2%) tested HIV positive. The age of patients ranged between 1 to 74, with most patients in age group 21–30 years. Of 218 isolates, 174 (80%) had spoligotype patterns previously found in the SpolDB4 database and 44 (20%) were unique. The major spoligotypes identified were the Haarlem lineage (19.7%), followed by the T (16.5%), LAM (9.1%), Beijing (7.3%), *M. africanum* West African 2 (6%) and Cameroun (5.5%) lineages. Patterns suggestive of mixed infections were identified in an additional 3.2%, such as the sole lack of spacers 33 and 34, suggesting a combination of Euro-American *M. tuberculosis* and the Beijing lineage.

Conclusion: The population structure of the *M. tuberculosis* complex in Dakar reflects a predominance of Euro-American *M. tuberculosis* (Haarlem, T and LAM), with lower prevalence of the Beijing lineage and *M. africanum* West African 2. The latter appears to have decreased in prevalence since reports from the 1970s based on biochemical speciation, which reported prevalence of *M. africanum* around 20% in Senegal.

ROLE OF MICROSCOPY IN THE DIAGNOSIS OF TUBERCULOSIS

PS-100076-15   Automated tuberculosis screening using image processing tools

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Aim: To automate the current Tuberculosis screening method (bacilloscopy) using image processing algorithms and low-cost hardware in order to free human resources and compensate for the lack of trained specialists.

Methods: 300 images were collected at the Hospital Nacional Dos de Mayo by manually adjusting a 7-megapixel digital camera (FE-270, Olympus Inc.) into one of the eyepieces of a binocular microscope (CX41, Olympus Inc.). Using a PC, each image was processed based on color information, edge detection and size to establish objects of interest. Some of these objects were filtered based in heuristics including size, eccentricity and color. The remaining objects were analyzed using shape features based on Hu and Zernike moments. Fukunaga's criterion was used to select the features which could better discriminate between bacilli and other objects. A Support Vector Machine (SVM) was trained with the selected features to classify the objects in 'bacilli' or 'not a bacilli'. These results were compared to manually segmented images which were considered as ground truth. These images were annotated by a technician with 15 years of experience.

Results: 298 bacilli and 366 other objects were found. Using Fukunaga's criterion, the perimeter of the bounding box, the area, the eccentricity, 2 Hu moments, and 4 Zernike moments of the object analyzed were selected for shape representation. The classification stage provided results over 92% in sensitivity.

Conclusion: This work provides a proof of concept on how image processing techniques can be applied to automatically detect bacilli with minimally low-cost changes to current setup (microscope). Better diagnosis accuracy can be achieved by building ad-hoc hardware and by improving the image acquisition procedure.

PS-100395-15   A role for fluorescent counterstains in combination with auramine-O LED microscopy?

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The recent introduction of LED based fluorescent microscope systems and recommendation of their use with the auramine O staining method by the WHO

will likely result in a change in microscopic protocols for many TB laboratories in the coming years. Various modifications of the basic auramine O staining method have been described that may have advantages in some situations with some forms of microscope. Microscopic systems based on mercury-vapour lamps invariably use epi-illumination, whereas LED based systems are available with either epi-illumination (via the objective from above) or transmitted illumination (from below). Epi-illumination leads to a high contrast between the stained bacilli and the dark background, but with transmitted illumination the contrast is less as the background is brighter and has visible structure. Although on this basis it might be expected that epi-illumination is clearly superior maintaining the focal plane with a dark background on scanty positives can be challenging; particularly for new users and probably increasingly so as microscopes age. With epi-illumination counterstaining with an additional fluorophore with a contrasting colour visible in the fluorescent channel can be used to aid focusing while maintaining the contrast. Suitable stains for this application were described in the mercury vapour lamp era, but now auramine microscopy is more feasible due to LED microscopy, they deserve renewed attention. For example weakly counterstaining the background with thiazine red produces a strongly contrasting red background with bright green bacilli when examined with the currently available blue LED microscopic systems. This allows the focal plane to be maintained in the fluorescent channel while scanning the slide for bacilli. We encourage potential users to consider this approach with respect to user acceptance and potential to improve the ease of locating acid fast bacilli on scanty slides.

PS-100861-15   Quality control in sputum microscopy among selected health centers in Manila

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The level of proficiency of the 29 sputum microscopists in the City of Manila and its associated factors was determined. This was done by distributing to the centers 'TEST' specimen prepared at the Public Health Laboratory in Quiricada, Manila. The microscopists processed and examined the test specimens together with the bulk of samples received by the center. The scheme was blinded and allowed for a more objective way of evaluating the actual performance of the 29 TB microscopists. 21 quality control specimen were sent in four batches and 6 out of these were sputum positive. Majority (69.0%) of the microscopists correctly identified all three positive specimen and 17.2% were able to identify all the 6 sputum positive samples. The mean score for the microscopic examination of

the 21 quality control specimen was 89%. All the smears were collected and graded as to quality of smear size, thickness, evenness and staining. Most of them have satisfactory level of proficiency in smear size, thickness, evenness and majority have above 90% score in staining. The accuracy of the microscopists and its relationship with associated factors like training, visual acuity and condition of the microscope was also determined. Based from the findings, they have only marginal bearing on the accuracy of the microscopists. The association between the knowledge, attitude and practices (KAP) of the microscopists and their level of proficiency was also determined. In this study, majority of the microscopists (52%) have adequate knowledge, 66% have good attitude, and 93% have good laboratory practices. It was found out that 29% of those with adequate knowledge got score above 90% as compared with 33% of those with fairly adequate knowledge, and the difference between them is not statistically significant ($P = 0.56$). With regards to accuracy and practices, 19% of those with good laboratory practices have accuracy of more than 90% as compared to 50% of those with fairly good practices.

PS-101047-15   Sputum concentration is useful for diagnosis of suspected smear-negative tuberculosis

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Background: Sputum concentration has been claimed to be a useful tool for diagnosis of tuberculosis, but its application in routine diagnostic workup remains unclear in currently available guidelines. We aimed to evaluate its utility specifically for diagnosis of smear-negative pulmonary tuberculosis.
Objective: To evaluate the diagnostic yield of the sputum concentration technique in patients with clinical suspicion of smear negative pulmonary tuberculosis.
Methods: We included patients with clinical suspicion of pulmonary tuberculosis and at least two negative smears for AFB. Sputum samples were concentrated and then analyzed with conventional Ziehl-Neelsen or Auramine-O staining. Diagnosis of tuberculosis was based on a positive culture for *M. tuberculosis*. Patients with contaminated culture results were excluded from the analysis.
Results: 661 patients were included. Out of these, 182 had positive culture results from which 57 (31.3%) were positive for the concentration technique. The agreement between both staining procedures (Ziehl-Neelsen and Auramina-O) was 84.99% (kappa =

0.90; $P < 0.01$). Although Auramine staining was slightly more sensitive than Ziehl-Neelsen concentration (30.8% vs. 27.5% of sensitivity respectively), the difference was not statistically significant ($P = 0.24$). **Conclusions:** Sputum concentration represents a useful tool for diagnosis of smear negative pulmonary tuberculosis, being able to detect around 30% of culture proven cases. Both Ziehl-Neelsen and Auramine staining techniques gave good results with high degree of agreement. It should be considered in the diagnostic workup of this condition, due to its low cost, scarce technical requirements and quick results.

PS-101283-15   Analysis of the diagnostic value of the addition of methylene blue as the last step in ZN staining

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Aim: Methylene blue is currently added as the last step in the ZN staining procedure to increase the contrast for the screening of Tuberculosis (TB). However this step increases the difficulty of automating the screening process using image processing algorithms. The aim of this work is to compare the TB diagnosis when methylene blue is added and when it is not.
Methods: Images from the slides of 8 patients with TB were acquired at the Hospital Nacional Dos de Mayo. Each slide was processed following the ZN staining but without adding methylene blue. 100 were taken at this point. Subsequently, the slide was rinsed, methylene blue was added and 100 more images were acquired. An expert technician, with 15 years of experience, annotated both sets of images. TB Diagnosis and number of bacilli are compared for both cases.
Results: The Table shows the results for the experiment. In all cases, the number of bacilli counted is higher when methylene blue is not added.

	# bacilli (diagnosis) with methylene blue	# bacilli (diagnosis) without methylene blue
Patient 1	154 (++)	654 (+++)
Patient 2	998 (+++)	1012 (+++)
Patient 3	19 (+)	263 (++)
Patient 4	17 (+)	460 (++)
Patient 5	143 (++)	715 (+++)
Patient 6	109 (++)	643 (++)
Patient 7	73 (+)	477 (++)
Patient 8	509 (++)	838 (+++)

Conclusion: We hypothesized that the several bacilli were washed out when the slide was rinsed, and therefore, the count of bacilli when methylene blue was added is lower. The study supports that the addition of methylene blue can be skipped in order to facilitate the use of image processing algorithms to count bacilli.

PS-101445-15   Should we read 100 or 300 microscopic fields before noting a scanty or negative result?

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Objective: National Tuberculosis Program recommends reading 300 microscopic fields instead of 100 as recommended by the IUAILD before noticing scanty or negative result. The aim of this study was to compare both microscopic readings at first and second serial sputum smears.
Methods: From May to June 2008, sputum smears of 552 TB-suspect patients were prepared and stained by hot Ziehl-Neelsen method as recommended by the IUAILD and the national guidelines. The research of acid-fast bacilli (AFB) was performed by two experimented biotechnologists. After reading according to the national guidelines (300 fields), a sputum smear of each patient was prepared by a third biotechnologist with another number, then stained and read by the previously biotechnologists according to method recommended by the IUAILD (100 fields). The results were analysed using SPSS 15.0 and the statistical difference between both readings interpreted by the χ^2 test. Supervision visits and rechecking were performed as external quality assurance.
Results: At first serial of 552 sputum smears, 69 (12.5%) and 59 (10.6%) read respectively according to the national and international recommendations were AFB positive, $P = 0.001$; 10 (1.8%) negative-smears on reading 100 fields and positive on reading 300 fields were scanty. At second serial sputum smears, 7 (1.4%) specimen from 483 patients with negative-smears on reading 300 fields at the first serial were positive, while there was nothing like winning on reading 100 fields, $P = 0.001$. Supervision visits and rechecking performed had not detected majors errors.
Conclusion: Reading of 100 microscopic fields promotes missed cases of TB in a context of scanty cases. Its application, especially in the case of co-infection TB-HIV could make the microscopic yield less interesting.

PS-101474-15   Microscopy as tuberculosis diagnosis method in a context of moderate prevalence of HIV infection

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Objectives: Direct microscopy remains the main method of tuberculosis (TB) diagnosis in most of the laboratories in developing countries. Its performance is the subject to criticism in TB-HIV co-infection. The

aim of this study was to assess its yield and the grading of acid-fast bacilli (AFB) serial sputum smears by comparing samples from adults TB new cases with and without HIV-infection.

Methods: Sputum smears of 200 patients (100 HIV-infected and 100 non-infected) were prepared and stained by hot Ziehl-Neelsen method. Acid fast bacilli (AFB) quantification was done as recommended by IUATLD. Patients were tested for HIV with their voluntary consent. The results obtained were compared using the χ^2 test. Supervision visits and rechecking were performed as external quality assurance.

Results: The first serial sputum smears diagnosed 89% TB-HIV-infected and 94% TB-VIH-uninfected cases. The additional yield of the second and third sputum smears diagnosed 10% and 1% among TB-HIV-positive versus 5% and 1% among TB-VIH-negative. Considering AFB quantification, the TB-HIV-positive patients were more scanty, and less positive 2+ and 3+ at the first ($P = 0.089$) and the second serial sputum smears ($P = 0.010$). No major errors exceeding the acceptance number predetermined by the National Tuberculosis Program were detected by the supervisor among the sample rechecked during the period of the study.

Conclusion: Direct microscopy, well done, can diagnose more than 90% patients with pulmonary tuberculosis, even in context of HIV infection. It has the benefit of priority in diagnosing patients who present a risk of contamination to the community.

PS-101549-15   Accurate and rapid culture-free quantification of *Mycobacterium tuberculosis* bacilli in sputum

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Accurate and rapid determination of bacterial burden in sputum samples obtained from tuberculosis infected individuals is an important tool to understand the disease, for evaluation of disease severity and for treatment response. Culture based methods are difficult to perform and enumeration can be inaccurate due to organisms that fail to grow and organism clumping. To overcome this we have developed a quantification method based on Real-time quantitative *16S rRNA* PCR that controls for RNA quality, amount and inhibitors. Using this assay we found that 100% and 98% ($n = 86$) of artificially *Mycobacterium tuberculosis* spiked sputums (10^7–10^2 bacilli) could be enumerated to within 1 $\log_{10}$ and 0.5 $\log_{10}$ of the original spike, respectively. Quantification of bacilli in sputum was performed on longitudinal samples collected, during the 6 month treatment period,

from 44 *Mycobacterium tuberculosis*-infected subjects. Of these samples bacilli were quantified for 99% (326 of 328) in the range 10^8 to 10^2 bacteria mL^{-1}. RNA was detectable in samples with up to 1000-fold loss/inhibition, with a detection limit down to 10^2 bacilli mL^{-1} sputum. Using data from this assay we found that bacterial number as calculated by *16SrRNA* concentrations followed a biphasic exponential decay curve that has been reported in patients using culture based methods, which is reflective of bacterial quantification using solid agar. This method will have considerable value in monitoring treatment response in practice or in clinical trials.

PS-101012-15   LED fluorescence can be used to demonstrate mycobacteria in fine needle aspiration biopsies

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Introduction: Fine needle aspiration biopsy (FNAB) is a simple, safe and effective method to investigate suspected mycobacterial lymphadenitis in children. Fluorescence microscopy can provide rapid mycobacterial confirmation. Light-emitting diodes (LEDs) provide a cheap and robust excitation light source making flouresence microscopy feasible in resource-limited settings. We evaluated the diagnostic performance of LED fluorescence microscopy on Papanicolaou (PAP) stained smears compared to the conventional mercury vapor lamp (MVL).

Methods: FNAB smears routinely collected from palpable lymph node masses in children with suspected mycobacterial disease were PAP stained and evaluated by two independent microscopists using different excitatory light sources (MVL and LED). Mycobacterial culture results provided the reference standard. A manually rechargeable battery powered LED power source was evaluated in a random subset.

Results: We evaluated 182 FNAB smears from 121 children (median age 31months; IQR: 10–67 months). Mycobacterial cultures were positive in 84/121 (69%) children. The mean sensitivity with LED (mains powered), LED (rechargeable battery powered) and MVL respectively was 48.2%, 50.0% and 51.8% (specificity 78.4%, 86.7% and 78.4%). Inter-observer variation was similar for LED and MVL (kappa = 0.5). In 3 smears from 2 children both microscopists visualized mycobacteria while the culture seemed falsely negative. The mean time spent reading a negative smear was 3.2 and 3.9 minutes with LED and MVL respectively.

Conclusion: LED fluorescence microscopy provides a reliable alternative to conventional methods and has many favorable attributes that would facilitate improved, decentralized, diagnostic services.

PS-100579-15   Automatic assessment of the degree of TB-infection using images of ZN-stained sputum smear

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Aim: Automatic assessment of the degree of TB-infection, by counting the number of mycobacteria (Acid Fast Bacilli or AFB) in images of ZN-stained sputum smear, irrespective of shape, beaded-appearance & clumped-presence.

Method: A data-base in the Hue, Saturation and Intensity (HSI)-space corresponding to the pixels in the images of ZN-stained sputum smear is formed. The algorithm automatically detects the presence, and counts the number, of Mycobacteria in a given image of the ZN-stained sputum smear, by the following steps: (i) colour-segmentation of candidate Mycobacteria in the HSI space, based on Mahalanobis distance—in conjunction with a divide & conquer strategy applied to the background. (ii) A proximity-test algorithm for handling beaded structures, (iii) size-constraints, and (iv) connected-component labelling.

Results: From a collection of 205 images of sputum smears (ZN-stained according to Revised National TB Control Program (RNTCP) guidelines—in conformity with the WHO standard) from 12 patients, 36 images (which included smears sent by RNTCP, Govt. of India, for training technologists as a part of a quality control program) were used for building the data-base i.e., clusters in the HSI space. The rest of the images were used for testing the efficacy of our algorithm. The counts, extracted automatically, were found to be very close to those assessed manually (Figure); the maximum difference was 4 (out of 23 AFB). Further,
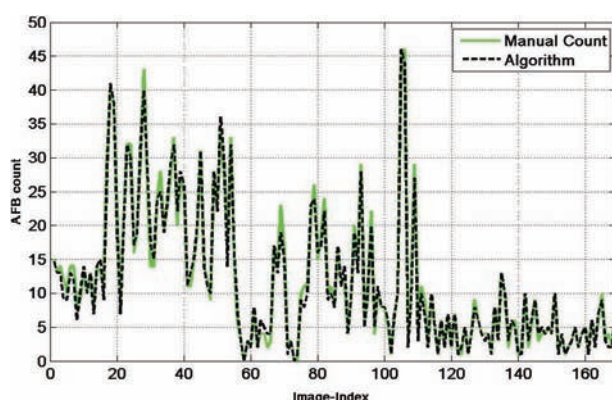
the percent correctness of identification of beadedness, and of the presence of clumps, was 81.77 and 85.40, respectively. The overall success of detecting Mycobacteria was 93.37%.

Conclusion: The method works well, and is simpler than those currently reported so far. It does not need shape-analysis (thus improving robustness), works irrespective of shape, beaded-appearance and detects Mycobacteria in clumps.

PS-101035-15   Improved polyacrylamide-based artificial sputum with cultured cell and formalin-fixed TB bacilli

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Background: We have developed polyacrylamide-based artificial sputum (PBAS) with cultured THP-1 cell and BCG-Pasteur strain (1st generation) and applied for panel testing and training of microscopists. While this PBAS is very useful and easy to prepare with grades (3+, 2+, 1+, ±, and negative), because unfixed BCG-Pasteur is used, the shape of bacteria is slightly different from the actual TB bacilli observed in the real sputum. Furthermore, it's sometimes difficult to pick up and apply the exact quantity in order to prepare smears of required grade because the bacilli had already mixed in viscous artificial sputum.

Improvement: In this study, we tried to develop improved PBAS with formalin-fixed TB bacilli to solve the problem in the 1st generation. Although the improved PBAS is prepared by similar protocol to the first generation, the formalin-fixed TB bacilli (H37Rv) are used and mix them on slide glass with prepared negative PBAS. Briefly, H37Rv was cultured with 7H9 broth with Tween 80, the fully grown bacillary solution was filtered with Acrodisk filter (pore size 5 μm) to disperse clumps of bacilli, then colony forming unit of the solution was enumerated with solid media and stored at -85 °C. On preparation of PBAS, the thawed bacillary solution was fixed and diluted with formalin to obtain required grades. 10 μl of the bacillary solution above was picked up and placed on slide glass, then, the negative PBAS was picked up and placed separately on the same slide glass. Mixed the bacillary solution with the PBAS and spreaded 1 $\times$ 2 cm or 2 $\times$ 3 cm ellipse.

Results and conclusions: With this improved artificial sputum, we only need to prepare negative PBAS and can adjust the positivity within the required grades by volume of bacillary solution applied, and the thickness of smears independent of the bacilli quantity. Furthermore, use of formalin-fixed TB bacilli provides great reality.

PS-101089-15   Evaluation of direct and concentrated smear microscopy for TB diagnosis in HIV prevalence setting

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Introduction: Direct and concentrated smear of sputum samples for AFB microscopy have been the most commonly used tools for diagnosis of TB. However, the sensitivity of the direct smear method, which is mainly used in the resource-poor countries is presently reported low especially in HIV-infected individuals. This study was therefore carried out to compare the sensitivity of the direct and concentrated smear methods for diagnosis of TB in both HIV-positive and negative individuals.

Method: The study population comprised of 480 patients drawn from the ARV and DOTS clinics in NIMR Lagos between 2008 and 2009. Two hundred and twenty-four (46.7%) of these patients were positive for HIV, 73 (15.2%) were negative while 183 (38.1%) had unknown status. Direct and concentrated smears of sputum samples obtained from the patients were stained by ZN and examined microscopically for AFB. Data was analyzed statistically using Prism version 5.03 computer software programme.

Results: AFB detection rates were 27.7% and 57.5% for HIV-positive and negative patients. In the HIV-positive patients, the AFB detection rates were 32 (14.3%) by direct smear and 75 (33.5%) by concentrated smear. In HIV-negative patients, 24 (32.9) were diagnosed by direct smear and 25 (34.2%) were diagnosed by concentrated smear. The rate of diagnosis by concentrated method was significantly higher than the direct method in the HIV-positive ($P < 0.05$) while there was no significant difference in these rates in the HIV-negatives.

Conclusion: Data showed a higher sensitivity in TB case detection by the concentrated smear method in the HIV-positive patients. About 43 patients amongst the group would have been missed if direct smear alone was carried out. The observation in this study highlighted the urgent need to develop capacity for concentrated smear in developing countries to be able to detect more TB amongst HIV patients.

PS-101120-15   Impact of three years EQA for AFB microscopy on the TB laboratories network performance in Mali

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Background: From 2006 to 2008 level of health centers increased from 2 to 3 and the number of microscopy centers from 66 to 77. Considering that DOTS strategy requires high quality TB laboratories network an EQA system was implemented in 2006 that relies on Blinded Rechecking and Supervisory visits coordinated by the NRL in Bamako.

Objective: To evaluate the performance of microscopy centers during a three years EQA process in order to come up with new recommendations and interventions for scaling up laboratory services.

Methods: Blinded Rechecking was implemented according to international guidelines and sampling by LQAS method. Detection proportional to controllers and percentage of true positives among all positives were calculated. Blinded Rechecking was supplemented with Supervisory visits conducted by NRL and District Hospitals.

Results: Blinded rechecking covered 65 of 66 microscopy centers in 2006, 68 of 70 in 2007 and 73 of 77 in 2008. Overall detection proportional to controllers increased from 0.89 in 2006 to 0.96 in 2007 and 2008 and percentage of true positives among all positives from 95% in 2006 and 2007 to 98% in 2008. The percentage of centers doing poorly decreased from 30.8% in 2006 to 13.2% in 2007 and 12.3% in 2008. Analysis by region was discussed. Supervisory visits allowed us to investigate problems. The most frequent of them was staff transfer to other health areas.

Conclusions: EQA by Blinded Rechecking over a period of 3 years resulted in an increase of detection relative to controllers at either national or regional level and a diminution of microscopy centers doing poorly. In this setting this improvement was likely due to training sessions and staff motivation linked to Blinded Rechecking. In addition, we conclude that more often the Supervisory visits were done more respect of national guidelines were observed. Staff transfer hampered the reliable functioning of the TB laboratories network. Recommendations were proposed.

PS-101181-15   Auramine microscopy diagnoses specific groups of TB patients who are not diagnosed by ZN microscopy

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Background: Fluorescence microscopy of auramine-stained sputum smears is quicker and more sensitive than Ziehl-Neelsen (ZN) microscopy for the detection of acid-fast bacilli (AFB). We quantitatively compared these techniques.

Method: Duplicate smears were made from 496 sputum samples. One was stained with ZN and read by

light microscopy, the other was stained with auramine and read by fluorescence microscopy on the same microscope. All smears were examined at ×1000 magnification, the number of AFB in 100 fields counted and geometric means calculated.

Results: Of 138 sputum samples positive by either method, the sensitivity of auramine was 99% (1 false-negative) vs. 73% for ZN (37 false-negatives, $P <$ 0.001). For samples positive by both methods, auramine detected an average of 2 more AFB per 100 fields than ZN ($P < 0.001$). Thus sputum samples with low auramine AFB counts were often false-negative with ZN. However some ZN false-negatives had high auramine counts (Figure). For ZN false-negatives, auramine detected an average of 40 more AFB per 100 fields than ZN ($P < 0.001$), suggesting that factors other than low bacillary load may explain some ZN false-negatives. In logistic regression, ZN false-negatives were independently more likely during treatment (OR 6.1, $P = 0.0001$), from patients with isoniazid-susceptible TB (OR 8.3, $P =$ 0.05) and for paucibacillary '+/−' sputum (OR 9.0, $P < 0.001$). Similarly in linear regression, excess AFB count in auramine increased with days of TB treatment ($P = 0.01$), increased as the AFB concentration decreased ($P = 0.03$) and tended to be greater for isoniazid susceptible samples. ZN false-negatives were not associated with rifampicin or multidrug resistance, sputum storage or viscosity or culture results.
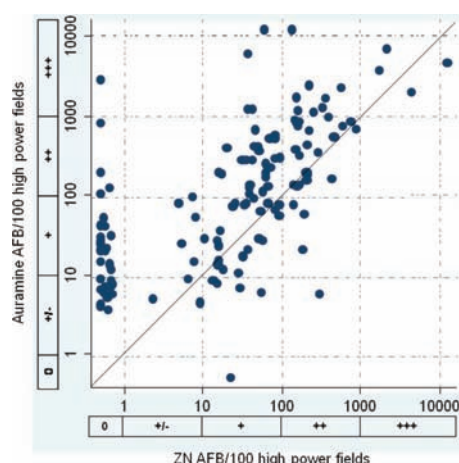
Conclusion: Auramine microscopy is more sensitive than ZN for paucibacillary sputum. In addition, sputum from patients with isoniazid-susceptible TB or collected during TB treatment are more likely to have TB detected by auramine microscopy than by the ZN technique.

PS-101264-15 Comparison of microscopy techniques in diagnosis of TB among smear-negative HIV patients in Uganda

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Introduction: There is an urgent need to develop low-cost diagnostic tools to enhance the accurate diagnosis of TB in patients with HIV/AIDS. TB incidence in Uganda is 369 per 100 000 per pop/per year with approximately 50% of identified TB cases co-infected with HIV. Sputum smear microscopy has a low sensitivity with a higher rate of smear negative pulmonary tuberculosis (PTB) in patients co-infected with HIV/AIDS. Indirect fluorescence microscopy (IFM) and analysis of concentrated sputum smears are credited with increased sensitivity and higher detection rates, but there is concern that specificity may be lower.

Methods: Prospective study carried out September 2008–July 2009. Sputum samples were obtained from patients with HIV/AIDS with suspected PTB on the basis of WHO clinical criteria. Initial smear microscopy by direct ZN at sample site were negative. Patients submitted two further sputum samples which were decontaminated according to the sodium hydroxide–N-acetyl-L-cysteine method and concentrated. A repeat Ziehl-Neelsen, IFM and MGIT were performed on the concentrated decontaminated samples. MGIT was the gold standard.

Results: 762 specimens were received from 381 patients. See the Table for comparison of the techniques against MGIT. Sensitivity of concentrated ZN method on previously 'sputum-negative' samples was 22.1% (9.7–39.6%) with specificity of 96.3% (93.7–98%). Sensitivity of IFM was 22.1% (9.7–39.6) with specificity of 96.6% (94–98.2).

Conclusions: Although ZN smears on concentrated sputum and indirect fluorescent microscopy perform better than traditional ZN microscopy, their sensitivity remains low.

Recommendations: IFM and concentrated ZN smears can be utilised in a low-income high TB prevalence setting to further aid rapid diagnosis of TB.

Table Results of concentrated ZN and indirect fluorescent microscopy compared to MGIT

	Mycobacterial growth indicator tube (MGIT)		
Concentrated ZN	Negative	Positive	Total
Negative	668	53	721
Positive	26	15	41
Total	694	68	762
Indirect fluorescent microscopy	Negative	Positive	Total
Negative	670	53	723
Positive	24	15	39
Total	694	68	762

PS-101325-15   Quality assessment of smear microscopy for acid-fast bacilli in Serbia, 2006–2009

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The external quality assessment (EQA) of smear microscopy for acid-fast bacilli (AFB) was introduced in the tuberculosis (TB) laboratory network in Serbia in 2006. The network currently includes 35 laboratories, which annually perform approximately 90 000 smear microscopy examinations. The EQA of smear microscopy consists of unblinded rechecking by a laboratory supervisor of positive slides and 10% of negative slides. Regional laboratories are supervised by the National Reference Laboratory (NRL), while peripheral laboratories are supervised by the regional or the NRL. The proportion of the laboratories included in the EQA increased from 51% in 2006 to 75% in 2009. Out of 6500 smears rechecked during the study period, smear quality was assessed as good in 87.4%, while the proportion of correctly stained smears was 96.2. The overall agreement in reading results among all supervising and supervised laboratories improved from 94.7% in 2006 to 99.2% in 2009. The proportions of false-negative results that ranged between 0% and 1.4% can be considered acceptable, but high proportion (8%) of false-positive results in 2006 prompted corrective actions such as procurement of new microscopes and training courses for laboratory personnel. The percentage of false-positive results reduced to 1.3% in 2009. The overall sensitivity per year varied from 99% to 100%, while the specificity significantly increased from 89.2% in 2006 to 98.5% in 2009. The major goals for the future are inclusion of all TB laboratories in Serbia into the process of EQA of smear microscopy and development of new EQA guidelines involving random blinded rechecking of AFB smears.

PS-100277-15   Added value of culture in the diagnosis of TB in smear-negative suspects in high HIV prevalence area

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Background: Western Kenya accounts for the highest TB and HIV prevalence rates in Kenya. In 2007, Médecins Sans Frontières in collaboration with the Ministry of Health set up a Mycobacterium culture laboratory in Homa Bay District Hospital with the aim of improving diagnosis of TB in HIV patients with smear negative results.
Methods: Retrospective study. Sputum culture was performed on Löwenstein-Jensen and Thin Layer Agar to all patients presenting with a cough for more than 2 weeks, at least 2 negative sputum smear microscopy and no smear positive result.
Results: From November 07 to December 09, a total of 2269 patients had a culture result available: 1664 (73.3%) were negative, 435 (19.2%) positive for *Mycobacterium tuberculosis* and 137 (6.0%) contaminated. In 33 (1.5%) patients atypical mycobacteria was found. Of the 435 patients with positive *M. tuberculosis* culture, 142 (32.6%) were started on anti-TB drugs at the hospital after receiving the culture result and 66 (15.2%) were traced and transferred to other health facilities to start treatment. Of the remaining patients: 142 (32.6%) had already been started on treatment prior to the culture result following clinical diagnosis algorithm, 29 (6.6%) had died, 42 (9.7%) could not be found and for 14 (3.2%) patients there was no information available. In total 15% of the 934 patients started on TB treatment at the hospital were initiated due to the availability of culture.
Conclusion: A considerable proportion of smear negative patients can be diagnosed of TB through culture. The availability of this technique may dramatically change the diagnosis strategy of TB in a high HIV prevalence setting. A prospective study comparing the diagnostic algorithms against the use culture is underway.

PS-100626-15   Cost-effectiveness of an immunochromatographic rapid test for the detection of active tuberculosis

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Setting: A novel immunochromatographic rapid test (ICT-Tb) was developed to improve the detection of active pulmonary tuberculosis (PTB).
Objective: To compare the cost and effectiveness between the use of smear microscopy (SM) as a diagnostic procedure versus the use of the ICT-Tb plus one SM for the diagnosis of PTB.
Methods: A decision model was developed using TreeAge Pro 2009*. Sensitivity and specificity data was based on the results of a previous clinical trial performed in 11 rural centers of the state of Veracruz, in Mexico, in 2005. The perspective of the study was that of the national public sector. Main outcome indicators were: number of cases avoided, years without disability and incremental cost-effectiveness ratios.
Results: A total of 372 subjects were included in the clinical study. 75 were eliminated due to different causes (lack of culture, SM or ICT-Tb), 48 (16.2%) were considered as contacts, 233 (78.5%) were diagnosed as chronic productive cougher and 16 (5.4%)

with active PTB. One SM had a sensitivity of 67.56 (95% confidence interval 56.9–78.23%); Specificity of 100% (95%CI 99.3–100%). The ICT-Tb sensitivity was 63.51% (95%CI 52.5–74.4%) and its specificity was 82.28 (95%CI 76.6–87.9%). The combination of ICT-TbP with one SM increases sensitivity to 93.2% and specificity to 99.4%. The use of the ICT-TB and one SM represents a higher cost, but decreases the transmission of the disease from PTB suspects and increases the total amount of years lived without disability. Cost-effectiveness ratio indicates that this new technology can generate one more year without disability for every 39 US Dollars invested in such setting.

Conclusions: The use of ICT-Tb and one SM is easier and more cost-effective than the use of SM alone as a diagnostic procedure to confirm PTB.

TB CONTACT TRACING AND OUTBREAK INVESTIGATION

### PS-101235-15   Household case contacts of patients with multiresistant tuberculosis in Kinshasa

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Framework: The Democratic Republic of the Congo is one of 27 high M (X)DR-TB burden countries. Each year are confirmed less than 100 isolates resistant to both the isoniazid and rifampicin among chronics cases. This study took place in Kinshasa, which provided 80% of MDR-TB cases.

Objective: This study was the early detection of cases of tuberculosis multidrug bacilli from family contacts of the patient.

Methods: Cases were listed through records of category 4 of the years 2005 to 2007 at the University Hospital of Kinshasa. Family and household contacts were interviewed and acceptance was driving to tests, chest X-ray, research BAAR on spontaneous or induced sputum (by hypersalines solutions inhalation). Sputum culture and DST in solid medium by indirect method at the Mycobacteriology laboratory of the University of Kinshasa clinical laboratory testing.

Results: A total of 140 index for 3 years; 49 in 2005, 42 in 2006 and 2007 49 cases. 564 cases contacts have been listed. An average of 4 family contacts. 296 were examined, 41 (13.85%) had a pathological image at X-ray, 14 cases had positive culture with *Mycobacterium tuberculosis* and 13 (92.85%) of them had an MDR-TB strains. Reported to all contacts examinated 13/296 (4.39%) was MDR-TB confirmed.
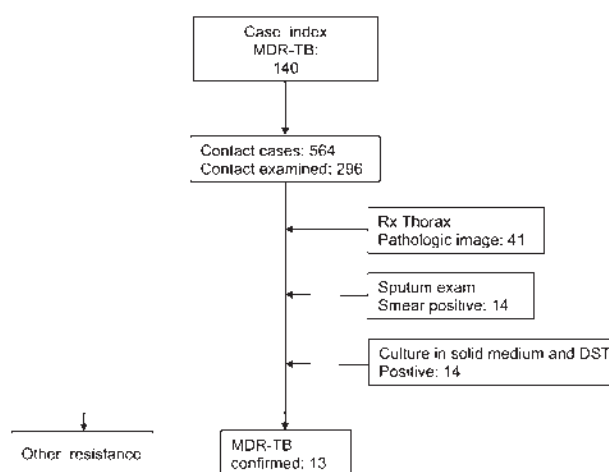
Conclusion: The systematic search for MDR-TB strains should be systematically among close contacts of MDR-TB patients. It is important that this figure among directives in low-income countries.

PS-100028-15   Nosocomial transmission of multidrug-resistant *M. tuberculosis* strains in a high-incidence setting

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Actuality: Delayed diagnosis of multidrug-resistant tuberculosis (MDR-TB) for in-patients treatment is an important problem in many TB hospitals, because it can contributed to nosocomial infection. However, the magnitude and reasons of TB nosocomial transmission are only insufficiently investigated, especially in developing countries with high rates of MDR-TB.

Aim: To assess the phenomenon of nosocomial transmission of MDR-TB between TB patients by investigation of *M. tuberculosis* DNA diversity using DNA fingerprinting. Study population was TB patient's new cases and retreatment's, who were on treatment in 4 TB hospitals from Moldova, during October 2007–April 2009.

Methodology: Epidemiological, microbiological, molecular-genetic methods. IS*6110* DNA fingerprinting was performed on pairs of isolates of *M. tuberculosis* from TB patients who became MDR-TB patients after 2–4 month of tuberculosis treatment.

Results: In total, *M. tuberculosis* strains obtained from 24 patients with pulmonary TB were investigated. Most patients had strains sensitive to all anti-tuberculosis first line drug (15 patients), or mono-resistant (5 patients) before treatment was started. Four patients had strains resistance on 2 drugs (SM and INH) at baseline. After 2–4 months of treatment all patients developed MDR-TB. DNA fingerprinting

analysis showed that 50% of the follow up isolates were different from those isolates obtained at baseline, indicating a significant level of exogenous re-infection presumably by nosocomial transmission.

Conclusions: Nosocomial infections appear to be a major cause of treatment failure by exogenous re-infection with MDR strains in an area with a high incidence of this disease. Hospitalizing of the patients with tuberculosis—whether it is drug-sensitive or drug-resistant—without of good infection conditions in hospital, puts them at increased risk of re-infection with MDR-TB.

PS-100342-15 'Inform and advise' in TB contact tracing: what constitutes success?

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Introduction and methods: Contact tracing individuals exposed to tuberculosis (TB) is an important component of UK TB control, though appears variably successful. This may reflect the methods used plus index case inability/reluctance to disclose exposed contacts, who then may not attend for screening anyway. Here we describe a specific exposure from one individual to a large family unit and explore its implications for contact tracing as described in NICE (2006) TB Guidance.

Results: A previously well 26 year old male Nigerian had stayed for eight weeks with relatives in a large house in London. For the last 10 days, he reported a productive cough. His CXR revealed extensive cavitation; and sputum smear was strongly AFB positive. He was admitted to hospital (day 0). Thirteen family members (ages 1 to 60) were screened over the next 12 days using NICE Guidance appropriate for age and BCG history with 2-step Tuberculin skin test (TST)—IGRA methodology. None were detected as having either latent TB infection (LTBI) or active tuberculosis. Three further subjects screened negative at day 40. Advice was given to all contacts to get in touch with the TB service if they developed symptoms. At day 89, a previously screened 10 year old presented with pulmonary TB. All contacts were re-screened, and others who had stayed with the index located. The results of re-screening are shown below. 7 contacts had active TB and 7 LTBI. The same organism was grown from 5 positive cultures.

Conclusion: NICE Guidance does not suggest an optimum time to screen contacts—and generally this is performed whenever they can be located. Early (day 12) IGRA testing may not be accurate. The most useful intervention, here, appears to have been use of 'inform and advise' to ensure that the family knew how to contact the TB service directly if needed. Baseline CXR for all ages and routine three month follow up should be considered.

PS-101243-15 Incorporating patient risk factors into tuberculosis outbreak prioritization

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Background: Genotyping (spoligotype + 12-locus MIRU-VNTR) of *Mycobacterium tuberculosis* isolates has been performed for over 38 000 patients in the United States. When genotyping information is combined with patient characteristics, including geographic location, automated searches can identify genotype clusters that may represent tuberculosis (TB) outbreaks. We conducted such an automated search and then analyzed patient risk factors to characterize clusters by the chance of future growth.

Methods: The software program SaTScan was used to identify TB genotype clusters in the United States during 2005–2008 with statistically significant geospatial concentration. Of these, we selected clusters where the beginning of the cluster could be identified (i.e., the cluster had no patients in 2005) and cluster growth could be observed for at least 3 years. This analysis focused on clusters with at least 3 persons; clusters were classified as those that grew or did not grow on the basis of having a fourth clustered patient in the 12 months after the 3rd patient.

Results: Of 65 clusters analyzed, 36 (55%) grew and 29 (45%) did not grow. Of 13 clusters where at least one of the first three persons was homeless, 12 (92%) grew. Of 23 clusters where at least one of the first three persons used excess alcohol or illicit drugs, 18 (78%) grew. Of 8 clusters where no person was sputum-AFB-smear positive, only three (38%) grew, and of 16 clusters where at least one person was Asian, only 5 (31%) grew.

Conclusion and recommendations: This analysis suggests that TB genotype clusters comprising patients who are homeless or use substances are more likely to grow into outbreaks. Using patient risk-factor data to estimate the chance of TB genotyping cluster growth can help public health officials intervene when clusters are still small, when TB transmission is most amenable to control measures.

PS-101030-15 A systematic approach to improving contact investigation activities in San Francisco

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Background: Contact investigation (CI), the investigation of contacts to persons with infectious tuberculosis (TB), is challenging operationally. CI requires multiple interviews, repeat screenings, decisions based on incomplete data, and defies simple algo-

rithms. Systematic evaluation of CI practices at the program level is needed to elucidate vital components. We systematically evaluated the activities of disease control investigators (DCIs) in San Francisco TB Clinic to develop and evaluate interventions to increase effectiveness.

Methods: We conducted baseline evaluations, developed, pilot-tested, and evaluated new interventions/ protocols, and measured overall impact. Baseline evaluation consisted of DCI interviews, meetings, and shadowing. We instituted a quarterly CI cohort review using standard national performance measures.

Results: Baseline evaluation revealed redundant paper systems and poor interface with the clinical database, discouraging timely data entry. CI knowledge was inconsistent among DCIs, without a forum to share knowledge or elicit assistance. New investigations were presented, activities prioritized and knowledge/strategies shared at weekly meetings. Forms, standards, and protocols were developed to standardize activities. Development of user-friendly database interfaces allowed DCIs to track incomplete investigations, organize tasks, and pre-populate forms. Performances were tracked using quantitative measures. Comparing 2006 (pre-intervention) and 2009 (post-intervention) performance, timely case interviews increased 40%, home evaluations increased 60%, and full evaluation of contacts increased 15%.
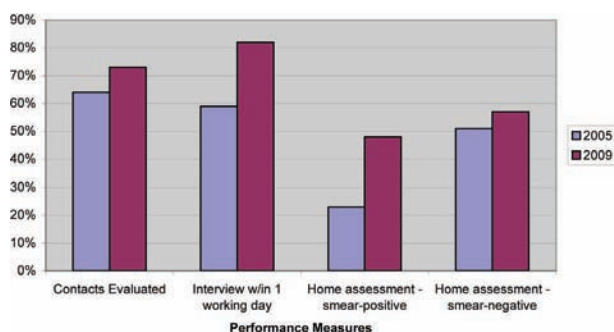

Figure SF TB contact investigation.

Conclusion: A systematic evaluation led to the development of standards, tools, and a database interface that tracked activities to aid in CI completion. Quarterly cohort review gave timely feedback to DCIs on their performance. CI activities have significantly improved and this is likely due to recently implemented changes.

PS-101103-15 Tuberculosis outbreak investigations in the United States: 2002–2008

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Background: To understand circumstances that strain public health resources, we characterize US TB outbreaks in which CDC was invited to provide epidemiologic assistance.

Methods: We systematically reviewed CDC staff reports and publications of US outbreaks in which CDC participated during 2002–2008, involving at least three culture-confirmed TB cases linked by both genotype and epidemiology.

Results: Twenty-seven out of total 51 TB investigations met the inclusion criteria (401 cases, 398 patients, median 10 patients per outbreak). Among outbreak patients, 364 (91%) were U.S.-born, 265 (67%) were African American, and 259 (65%) were male. Of 122 (84%) with pulmonary disease, 201 (60%) were acid-fast bacilli smear positive and (37%) had cavitation. Most common TB risk factors were substance abuse (58%), incarceration history (32%), and homelessness (20%). Fourteen outbreaks involved at least 50% patients who were U.S.-born males with substance abuse. The most frequent outbreak contributing factor was delayed diagnosis (12 outbreaks) and incomplete contact investigation (10). Drug-use locations (17 outbreaks [63%]) were identified as the most common locations associated with transmission, followed by homeless shelters (5 outbreaks [18%]). Prioritized screening of contacts based on TB risk, healthcare worker education, and location-based screening were most frequently cited interventions.

Conclusions: Although foreign-born persons bear a disproportionate burden of TB, transmission in U.S.-born sub-populations involving substance abuse threatens TB elimination in the United States. Strategies to enhance early diagnosis, screening, and treatment adherence in these populations are needed.

PS-101344-15 Investigation of a tuberculosis cluster in a college

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Background: Tuberculosis (TB) remained an endemic infectious disease in Taiwan with the incidence of 63.2 per 100 000 persons in 2007. TB cluster in school setting poses a major public health challenge. A cluster of TB in a college, with most patients related to the wrestle team, was reported in 2008.

Methods: Contact investigation was conducted to identify close contacts and potential transmission routes. Information of case patients were collected from medical records and the National TB Registry. *Mycobacterium tuberculosis* isolates were genotyped with IS*6110* restriction fragment length polymorphism (RFLP), mycobacterial interspersed repetitive-unit-variable-number tandem-repeat (MIRU-VNTR) and spoligotyping. Annual chest radiographic examination was implemented in the college to find new TB patients. Any latent infected member in the wrestle team, identified by tuberculin skin test, was under direct observed prophylaxis.

Results: From May 2006 to Oct 2009, nineteen TB patients were notified. Of the nineteen patients, seven were diagnosed with respiratory symptoms at health care facilities, eight through annual chest radiographic examination campaign, two through contact tracing and two through health examination. Twelve were culture-positive cases. Of these 12 *M. tuberculosis* isolates from respective 12 wrestlers, eleven isolates had identical spoligotypes, RFLP and MIRU-VNTR patterns. Among the 53 wrestlers, 24 had a diameter of tuberculin induration > 10 mm. Wrestlers recruited after 2006 had significant higher risk of tuberculin induration > 10 mm than those before 2006 (OR, 14.40; 95%CI, 3.24–68.48; $P < 0.001$).

Conclusion: Due to close contact with an active TB case during sport training, TB transmission was identified in a wrestler team.

PS-100530-15   Impact of active case finding among household contacts of TB patients on case detection rate in Afghanistan

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Introduction: Under circumstance with high incidence of smear positive TB, risk of development of active TB among household contacts is very high, due to cultural issue, such as crowed population in small houses. However, there has been no consolidated contact management.

Objective: To assess the impact of active case finding strategy in a high prevalence population in Afghanistan.

Methodology and setting: A cross-sectional analytic study was conducted from Nov. 2007 to Oct. 2008 in four randomly selected provinces (Parwan, Jawzjan, Laghman and Heart). 2837 Household contacts of 510 SS+ TB patients aged more than 15 years interviewed and identified suspects were screened for TB by sputum sample microscopy.

Results: Among 2837 household contacts, 340 cases (12%) showed pulmonary symptoms and out of these, 112 cases had cough more than two weeks and 33 (29%) of these cases had productive cough. Finally,

sputum smear examinations revealed 5 SS+ cases. The prevalence of SS+ TB in household contacts of a TB patient is 5 per 2837 (0.2%).

Conclusion: The prevalence of SS+ TB among household contacts of TB patients (176 SS+/100 000) is considerably higher than the estimated rate in the general population (76/100 000). This results indicate significant impact of active case findings among household contacts.

TB IN SPECIAL POPULATIONS

PS-100245-15   Primary drug-resistant tuberculosis in prison institutions of St. Petersburg, Russia

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Background: Morbidity with tuberculosis (TB) and prevalence of drug resistant TB among prisoners worldwide are significantly higher than in civil population.

Setting: Central prison hospital in St. Petersburg, Russia.

Study design: We retrospectively reviewed case records of 196 patients with new culture-positive TB cases, who were admitted for in-patient treatment between January 1, 2005 and September 30, 2009. We used method of absolute concentrations in Löwenstein-Jensen medium to determine *Mycobacterium tuberculosis* resistance to Isoniazid (H), Rifampicin (R), Ethambutol, Streptomycin, Kanamycin and Ofloxacin. *M. tuberculosis* isolates were divided into groups by susceptibility: pan-sensitive, resistant to one or several drugs, but not H+R (DR), multidrug-resistant (MDR). There were also eight extra-drug resistant (XDR) TB isolates detected: one in 2007, four in 2008 and the remaining in 2009. We considered them as a part of MDR group. We reviewed annual distribution of the study groups, see the Table.

Results: We observed consecutive increase in annual occurrence of primary MDR-TB cases between 2005 and 2009 ($P = 0.00034$).

Conclusions: During the last five years, the increase in value of primary MDR-TB among prisoners in St. Petersburg region was observed. Introduction of the fast methods of *M. tuberculosis* cultivation and drug susceptibility testing in prisons of St. Petersburg is required.

	2005	2006	2007	2008	2009†
Pan-sensitive, %	17/48.6	17/47.2	5/20.8	13/29.5	18/31.6
DR, %	10/28.6	6/16.7	11/45.8	6/13.6	5/8.8
MDR, %*	8/22.9	13/36.1	8*/33.4	25*/56.8	34*/59.6

* Including XDR-TB isolates.
† January–September 2009.

PS-101190-15   Diabetes mellitus among multidrug-resistant TB patients in four Asian countries

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Background: The Preserving Effective TB Treatment Study (PETTS) is a multi-country prospective study of MDR-TB that aims to determine the frequency of, risk factors for, and consequences of acquired resistance to second-line TB drugs (SLDs). DM is a growing concern in Asia, associated with TB risk but lacking a well-established association with MDR-TB.
Objective: To determine differences in baseline characteristics and outcomes of MDR-TB patients with and without DM in the Philippines, South Korea, Taiwan and Thailand.
Methods: From March 2005 to June 2008, we collected demographic, clinical and laboratory data on consecutive consenting adults with pulmonary MDR-TB starting SLD treatment and followed them with monthly sputum cultures, comparing characteristics and WHO-defined outcomes of patients with and without DM.
Results: By March 2010, 521 patients had treatment outcomes. DM was the most common medical comorbidity, noted in 133 (25.5%). Patients with DM (vs. without DM) were older (mean age 48.3 vs. 36.2 years, $P < 0.01$), more likely to be married or cohabiting (105 (79%) vs. 220 (57%), $P < 0.01$), have BMI > 18 kg/m2 (113 (85%) vs. 181 (47%), $P < 0.01$) and have prior SLD treatment (30 (23%) vs. 44 (11%), $P < 0.001$). They were less likely to be admitted to a TB housing facility (6 [5%] vs. 45 [12%], $P < 0.012$). No significant differences ($P > 0.05$) were noted in rates of cure (64.7% for DM vs. 68.8% for non DM), default, death and failure; and in sex, education, employment, hospitalization, HIV status, baseline sputum smears, DST results, chest X-ray findings, waiting time to MDR-TB treatment, time to sputum conversion and occurrence of reversion.
Conclusion: Treatment outcomes did not significantly differ among patients with and without DM. DM is common among MDR-TB patients. Properly diagnosing and treating TB in patients with DM and DM in MDR-TB patients is imperative especially in view of the association between DM and prior SLD treatment.

PS-100572-15   Drug-resistant pattern of *Mycobacterium tuberculosis* isolates from elderly patients in Taiwan

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Background: To investigate the prevalence of drug resistance in *Mycobacterium tuberculosis* isolates recovered from elderly patients.
Methods: This retrospective and laboratory-based surveillance study was performed in a tertiary care center. Data on the prevalence of drug resistance in clinical and non-duplicate isolates of *M. tuberculosis* recovered from patients aged ≥65 years from 2000 to 2008 were evaluated. Susceptibility testing to anti-tuberculosis agents including isoniazid (INH), rifampicin (RIF), ethambutol (EMB), streptomycin (SM), rifabutin, ofloxacin, ethinamide and para-aminosalicylic acid was performed using the modified proportional method.
Results: Among the 3186 nonduplicate *M. tuberculosis* isolates found during the study period, 1497 isolates were recovered from elderly patients. Thirty-eight (2.54%) isolates were multidrug-resistant (MDR-TB). Significant decreasing trends in resistance rates to EMB, SM, at least anyone of the four first-line agents (ADR), and MDR-TB were observed. There was no significant difference in drug resistant pattern between the elderly (65–84 years) and very old patients (≥85 years), but the rates of resistance to INH, RIF, EMB, SM, ADR and MDR were significantly lower in isolates from the elderly than from adults (15–64 years old, $n = 1689$) (Table).

Table   First line drug resistance rate for *M. tuberculosis* isolates from adults (15–64 years old) and elderly patients (≥65 years old) using the modified agar proportional method

Agent (concentration [μg/mL] tested)	No. of isolates (%) from each indicated patient population		
	Adults ($n = 1689$)	Elderly ($n = 1497$)	*P* value
Isoniazid (0.2)	266 (15.8)	172 (11.5)	<0.001
Rifampin (1)	120 (7.1)	47 (3.1)	<0.001
Ethambutol (5)	149 (8.8)	78 (5.2)	<0.001
Streptomycin (2)	191 (11.3)	120 (8.0)	<0.005
Resistant to any drug	413 (24.5)	254 (17.0)	<0.001
Multidrug-resistant	97 (5.7)	38 (2.54)	<0.001

Conclusions: Although a decreasing overall trend of anti-TB drug resistance was found in the elderly and elderly patients had a lower rate of anti-TB drug resistance than adults in recent years, the higher rate of MDR-TB in Taiwan continues to present a challenge for the control TB in the elderly.

PS-101346-15   Vulnerable nomadic populations TB diagnosis and treatment in Afghanistan

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Nomad locally named 'Kochi' is a tribe that has no permanent residency, they are primarily sheep raisers who live in tents and travel seasonally. The total population of Kochis is estimated to be about 1.5 million in Afghanistan. The lifestyle and culture of nomads put them at risk for getting Tuberculosis. All family members live under the same tent, and often consuming raw milk. Given this, Kochis are considered to be vulnerable segment of Afghan. The hardships that Kochis' are enfaced in their settlement areas make health services inaccessible for them. Their tents don't have enough ventilation. Their poor nutrition status accelerates the development of disease. Kochis also don't have access to education and safe drinking water. For 100 Kochi households one individual is trained to facilitate DOT. S/he ensure timely intake of anti-TB medicine, trace the TB patients and identify TB suspects for sputum microscopy. The mapping contains information on number of households and approximate length of stay of each Kochi community. It forms the basis for identifying appropriate sites/locations for conducting outreach smearing sessions. Each 100 household is considered one outreach smearing site. Each outreach smearing site is covered once in a week. The DOT facilitators collect the sputum from TB suspects and bring it to the outreach searing sessions. Slide smearing is done at the field and microscopy examination is carried out at the microscopy centres. Suspects with positive results are informed for initiating DOTS at the health facility which is followed up by the DOT facilitators. This is an unique approach has been initiated in this country ever.

PS-100113-15   Pulmonary TB among elderly patients: higher rates, difficulties for diagnosis and poorer prognosis

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Background: Tuberculosis (TB) rates among the elderly (>65 yrs) in Mexico (31/100 000) are two-fold those among general population representing a major challenge to health systems. Complicating factors include immunosenescence, chronic diseases, and other infectious diseases.
Objective: To describe clinical and epidemiological consequences of pulmonary TB among the elderly:

Methods: We screened persons with more than 2 weeks cough in southern Mexico from March, 1995 to December, 2008. We collected clinical and mycobacteriological information (isolation, identification, drug-susceptibility testing and IS*6110*-based genotyping and spoligotyping) from individuals with bacteriologically confirmed pulmonary tuberculosis. Patients were treated in accordance with official norms and followed to ascertain treatment outcome, retreatment, and vital status. We present data for two age groups (45 to 64 years and 65 and more). We compared TB incidence and mortality rates. We used Cox proportional hazards models to assess the association of elderly age with death due to TB.
Results: 526 TB patients were older than 45 years of age; of these, 173 (33%) were 65 yrs of age or older. Individuals > 65 yrs had higher rates of recently transmitted TB rates, fewer symptoms and fewer bacilli in sputum as compared with 45 to 64 year old adults. Elderly age was associated to death due to TB (HR = 3.41; IC95% 1.4–8.3; P = 0.007) adjusting by gender, drug resistance, retreatment and diabetes.
Conclusions: Although high, TB rates among the elderly are most probably underestimated. Pulmonary TB among >65 years entails difficulties for timely diagnosis and poses a higher risk of mortality due to TB. Specific strategies to achieve timely diagnosis and treatment are needed for vulnerable group.

PS-100504-15   Tuberculosis among adoptees to the United States from China

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Background: Each year, more than 10 000 children from international locations are adopted by US parents. China, the largest source country for intercountry adoptions to the United States (3001 during fiscal year 2009) and has a high tuberculosis (TB) rate (98 per 100 000). According to US immigration law, intercountry adoptees are required to undergo screening for TB. Since July 2009, TB screening in China has included tuberculin skin tests (TST) for adoptees 2–14 years of age, chest X-rays for those with positive TST, and sputum cultures for persons suspected of having TB disease.
Methods: Data were reviewed from adoptees screened at Guangdong International Travel Healthcare Center from July 2009 through February 2010 to determine the rate of TB disease among US adoptees from China.
Results: From July 2009 through February 2010, 2104 adoptees were screened; 949 were 2–14 years of

age and received a TST, 143 (15%) had TST ⩾ 10 mm. Four TB cases were diagnosed (rate 190 per 100 000). Ages ranged from 2 to 8 years; all were sputum or gastric aspirate smear negative at diagnosis. Two children were culture positive (ages 2 and 8). The 2-year-old was gastric aspirate culture positive and drug susceptibility testing results demonstrated multidrug-resistant tuberculosis (MDR-TB).

Conclusion: Intercountry adoptees from China have a high TB rate and can have MDR-TB. Cultures of sputum and gastric aspirates should be performed on adoptees suspected of having TB.

PS-100508-15   Caracterización del estado de infección y enfermedad en adultos privados de libertad en dos centros

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Purpose: Determinar la situación de la TB en los Centros de Rehabilitación (CR) en una provincia de Ecuador, a partir de datos del estado de infección tuberculosa en las Personas Privadas de Libertad (PPL).

Methods: Estudio de prevalencia en 220 PPL, se aplicó tuberculina RT—23 (PPD 2UT). Se recolectaron 3 muestras para baciloscopia a los sintomáticos respiratorios identificados (SRI), además cultivo y prueba de sensibilidad. Se calculó el estimador puntual de prevalencia de la tasa de positividad para el estado de infección y TBP BK+ considerando una distribución binomial. Se cuidó aspectos éticos de consentimiento y confidencialidad.

Results: PPL entre 19 a 65 años. Tiempo promedio de reclusión 22 meses. 16 PPL por celda. Antecedentes de contacto con persona con TB 86 (39.1%). Uno

(0.4%) refirió tener VIH. Se encontró 31 (14.1%) SR (IC95% 9.5%–18.7%). Una tasa de positividad de TBP BK+ entre 219 PPL de 0.5% (IC95% 0.45%–1.8%) y de 4.1% (IC95% 4.1%–12.5%) entre los SR examinados. Se aplicó PPD en 149 PPL (67.7%), presentaron reacción mayor a 10 mm 132 (88.6%). La PVVS tuvo una reacción de 21 mm. La tasa de positividad del estado de infección por TB fue de 60.0% (IC95% 52.3%–67.7%). Entre las PPL con PPD positivo, 109 (82.6%) recibieron BCG al nacimiento. Las PPL con contacto con persona con TB 44 (88.0%) tuvieron PPD positivo, PPD positivo en 23 (88.5%) de 26 SR.

Conclusions: Se evidenció la vulnerabilidad de las PPL y la necesidad de reforzar la coordinación entre sistemas.

PS-100865-15   Gender and immigration issues: a 20 year TB survey in Milan, Italy

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Setting: The Regional TB Reference Centre at Villa Marelli Inst, Milan.

Survey: 7580 active TB cases treated from 1/1/1990 to 31/12/2009. Of them 2466 were Italians or from established economies (I), 5114 immigrants from high TB prevalence areas (Ix). 3.3% were HIV+ and 92.1% were new cases. 5670 and 1910 were respectively thoracic (exluding pleural) and extra-thoracic TB cases. Treatment Outcome (TO) was favourable on 94.2% of cases.

Methods: Clinical patterns were analyzed according to sex (M,F) and immigration.

Results: Ix of both sexes increased in the considered period from about 20% to 65% and their mean age is significantly lower (Ix F 37 vs. IF 50 yrs; IxM 36 vs. IM 61 yrs: $P = 0.004$). Among males (1025 I, 2360 Ix) no significant differences were observed in disease localization (extrathoracic TB: IxM 21.8 vs. IM 23.7%) or HIV incidence (4.8%) but an unfavourable TO was significantly more frequent among Ix than I males (14% vs. 10%, $P = 0.01$). IM were more likely to receive a patient-tailored regimen (11.5% vs. 6.9%). Among female (1122 I, 2090 Ix) no significant differences were observed in TO (94 vs. 92% favourable) but Ix F were more likely HIV+ (1.9% vs. 0.9%, $P = 0.03$). IF had instead significantly more often an extrathoracic TB (41% vs. 29.1%, $P < 0.005$) and a non-standardized treatment (11.5% vs. 6.9%).

Conclusions: Treatment modified from standard in IM and IF seems connect with older age, comorbidity
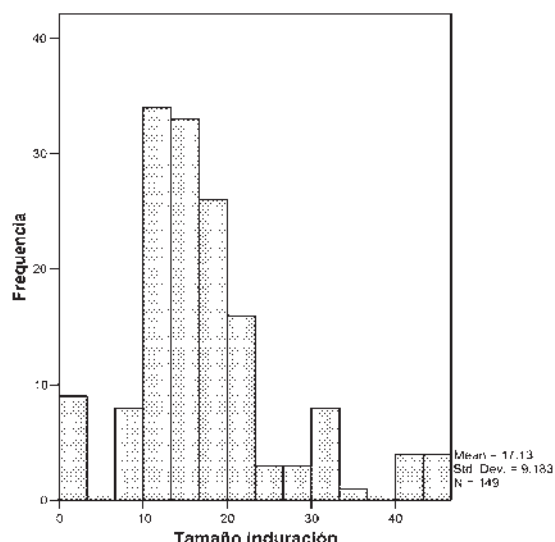
and intolerance to 1st line drugs; African origin is strictly correlated to HIV in IxF (65.5% vs 18.7% in overall pop.) Negative TO in IxM is instead related to poor social condition and concomitant risk factors ($P = 0.01$).

PS-100917-15 Evaluation of tuberculosis risk in a big university hospital of Havana City, 2009

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Objectives: To evaluate individual and collective tuberculosis infection risk by areas/occupational groups in the Calixto García University Hospital.
Patients and methods: Individual risk was measured in health care workers (HCWs). An interview to explore personal data, labor location and exposition to *M. tuberculosis* in its different grades and forms was applied. From the total 318 HCWs evaluated, a tuberculin skin test (TST) was underwent to 307; 254 were read 72 hours later. A 10 mm cut-off point was used. Individual risk was classified as high, intermediate, low and minimum. Collective risk was measured in each area/ department using individual risk, prevalence of latent tuberculosis infection (LTBI), tuberculin conversion rate and number of TB cases assisted per year. As well collective risk was classified as high, intermediate, low, very low and minimum risk.
Results: 58.8% of the surveyed HCWs have been more than 5 years working in this hospital; just 6 had a previous positive TST. Out of the 20 previously negative, 25% converted to positive. The prevalence of LTBI was 27.6% (70/254), the highest in service HCWs (33.9%) and the lowest in non health technicians (0%). Almost a quart of departments/areas (9/37) were evaluated as high risk, 37.8% as intermediate risk, 21.6% as low risk, 8.1% as very low risk and also 8.1% as minimum risk.
Conclusions: TB infection risk for the staff of the University Hospital Calixto García was between low and intermediate. Areas more at risk were urgencies and special care units as well as diagnostic laboratories.

PS-101032-15 Tuberculosis trends in Germany with a special focus on migrants

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Aim: To show trends and the potential impact of migration on the tuberculosis (TB) epidemiology in Germany.
Methods: Descriptive analysis of case-based notifica-

tion data received at the Robert Koch Institute (RKI) for 2002 to 2008 according to nationality, country of birth, demographic characteristics, drug resistance and treatment outcome.
Results: Since 2002, TB case numbers declined from 7667 to 4543 cases in 2008 (incidence 9.3 to 5.5 per 100 000 population). The corresponding reduction of 40.8% differed considerably between German and foreign nationals (41.8% vs. 36.1%, respectively). In 2008, TB incidence in foreign nationals was 5.3-times higher than in Germans. These differences were particularly found in young adults and in infancy. 44.0% of all cases were born abroad, most of them in one of the Newly Independent States (NIS) of the former Soviet Union (8.6%), followed by Turkey (6.4%). The proportion of drug resistant tuberculosis has stabilized in the last 3 years but remained higher in foreign borns—particularly in patients originating from the NIS (multidrug-resistant TB: 10.0% vs. 0.6% in German born cases). Despite higher resistance rates, treatment success rates were higher in foreign born cases (87.9% vs. 77.2% in Germans). This may be partly explained by the younger age structure in foreign born patients (median age 37 vs. 57). 85.2% of the not successfully treated Germans have died due to TB or other causes, while in foreign born patients the proportion of death was only 59.3%. However, foreign born patients showed an almost 3-times higher proportion of treatment interruption or defaulting.
Conclusion: Despite falling case numbers, tuberculosis still presents a public health problem in Germany, particularly in view of specific risks of treatment interruption and drug resistant TB in migrants. Thus, epidemiological characteristics in migrant TB patients need to be better understood in order to optimise TB management in Germany.

PS-101037-15 Study of tuberculosis of foreigners in Japan

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Aim: Foreigner (immigrant) patients with *Mycobacterium tuberculosis* are recently increasing in Japan. Especially, there are many foreigner patients with TB from Asian countries. More than a half of TB patients in USA and Europe (England, Germany) are foreign TB. In the near future, it will be estimated that similar situation (many foreign TB patients) will be problem in Japan. Therefore, the investigation study to regulate the foreigner patients with TB was done.
Methods: The investigation documents about the immigrant patients with TB were made and sent to

all Japanese public health centers and TB hospital (total 800).

Results: After receiving the answer for the documents, we analyze 2000 immigrant TB patients between 2006 and 2008. 20–30 years old immigrant TB patients from China, Philippine, Korea, Indonesia and Brazil were the largest number in Japan. Most patients had TB in 1–3 year after coming to Japan. Incidence of multidrug-resistant TB was 4.7%. There were many students, full-time employment patients with diabetes mellitus, in immigrants with TB. A barrier for language is found to be a big problem in these immigrant TB patients.

Conclusion: These data indicate that incident of multidrug-resistant TB was 4.7% in immigrant patients with TB in Japan. The number of immigrant TB patients from Philippine and Brazil is increasing. In San Francisco, QFT diagnosis system is able to decrease the number of immigrant TB patients. QFT may be applicable to immigrant TB patients in Japan.

PS-101224-15 Transmission of tuberculosis among native and immigrant populations: a systematic review

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Background: Genotyping of *Mycobacterium tuberculosis* provides information on recent Tuberculosis (TB) infection. We aimed to investigate dynamics of TB transmission between TB high-prevalence immigrant and TB low-prevalence local population in the European Union (EU) based on published molecular epidemiological studies by analysing the composition of mixed clusters, defined as clusters including foreign and native-born patients.

Methods: We searched for English-language published articles in Pubmed-database until February 2010. After screening 5900 citations 13 studies conducted in EU reporting on mixed clusters were included.

Results: 3 studies were nation wide (Norway, Western Sweden, Netherlands); 3 regional (Almeria, Spain, Baden-Württemberg, Germany, Limousin Region, France), and 7 urban (Bruxelles, Capital Region, Belgium; Barcelona, Spain, Hamburg, Germany, Madrid, Spain, Milan and Brescia, Italy, North-West London, UK, Zaragoza, Spain). 12 687 TB culture positive subjects (range 118–4266, median 530) were fingerprinted mainly by RFLP IS*6110* over a median study duration of 48 months (range 12–148). Median percentages of immigrants and autochthonous were 42.0% (ranging from 17.6% in Zaragoza to 79.7% in North-west London) and 60.9%, respectively. Clustered subjects were 4679, where immigrants accounted for 46.2% (mean), with relevant differences

among studies (range 11.3–84.8). Over 559 clusters, 23.3% were mixed, composed of a mean percentage of 40.5 of immigrants. Only 9 studies reported complete data on mixed clusters composition: out of 1950 autochthonous subjects, 45.5% were involved in mixed clusters and 54.5% in 'only autochthonous' clusters; similarly, 47.8% and 52.2% of 1645 immigrant patients were part of mixed or 'only immigrant' clusters.

Conclusions: Available data indicate similar risk of being part of mixed clusters for both populations and suggest transmission of recent TB between immigrant and autochthonous populations.

PS-101449-15 Evaluation of a binational tuberculosis referral program, 2009

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Background: CureTB is a binational referral program that enhances care by increasing completion of treatment, decreasing new infections, and preventing drug resistance for tuberculosis (TB) patients and their contacts who cross the Mexico–U.S. border. The program tracks types of referrals and patient outcomes.

Methods: We reviewed program guidelines, observed operations, and used focus-group discussions and interviews with key informants to assess program implementation issues. We created and calculated outcome evaluation indicators retrospectively using data from the referral log and operational documents for 2009.

Results: Referral services were provided to 49 (77%, $n = 63$) eligible TB patients and 8 (100%, $n = 8$) latent TB infections. All eligible health information requests ($n = 39$) were filled, serving 57 jurisdictions in both countries. We identified operational gaps which were due, in part, to inconsistent and irregular training as well as limited human resources. The evaluation was limited due to a lack of process and outcome data. CureTB revised and implemented new guidelines and referral criteria during the period under evaluation. CureTB staff report that scarce funding and personnel turnover has impeded their ability to address program goals and that insufficient coordination between stakeholders and partners has contributed to barriers in providing adequate and timely referral services.

Conclusions: Cure TB has developed expertise in binational referrals. We recommend that (1) stakeholders should articulate long-term binational TB program goals to improve CureTB's program effectiveness; (2) CureTB should standardize protocols to address gaps in program operations; and (3) CureTB should implement a monitoring and evaluation sys-

tem which captures key operational data to inform program planning and implementation and to evaluate achievements.

PS-100737-15 Investigation for tuberculosis outbreaks in congregate and health care settings in Taiwan, 2008

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Background: Identifying tuberculosis (TB) clusters in congregate or health care facilities is essential for treatment and interventions to interrupt transmission. A study of suspect TB clusters of congregate and health care settings detected in 2008 was conducted to find the factors associated with confirmed or probable TB outbreaks.

Methods: All TB clusters reported during January–June 2008 were included. A TB cluster was defined as one confirmed TB case with a subsequent suspect case in the same facility within one year. A confirmed outbreak was defined as having at least two patients' isolates with matching genotypes and known epidemiologic links. The characteristics of facilities, demographic data, clinical presentations of residents or workers with confirmed TB were obtained.

Results: In 2008, there were 47 suspicious TB clusters, occurring in respiratory care ward (9, 19.1%), nursing home (8, 17.1%), long-term care facility for minor impairment of self-care patients (27, 57.4%), hospital (3, 6.4%). Two were confirmed outbreaks (4.3%). Another four were probable clusters because there were no isolates available for genotyping though epidemiologic linkages exist. Of the other 41 clusters, five were non-TB Mycobacteria (NTM) related (12%). Among 71 suspect TB patients with positive sputum acid fast stain, 34% received NAAT test (positive predictive value (PPV) = 80%; negative predictive value (NPV) = 100%). The factor associated with confirmed or probable clusters was having a TB case in the institute of a respiratory care ward or nursing home (Odds ratio = 4.3, 95%CI: 1.2–15.1).

Conclusion: The NPV of NAAT is excellent to rule out smear positive suspect TB cases from suspicious clusters. The TB patients from an institute of respiratory care ward or nursing home was needed for early detection of suspicious outbreaks and implementation of the control measures to stop TB transmission.

PS-100291-15 Tuberculosis control in prisons: impact of intensive education and screening at entry

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Background: Tuberculosis (TB) control in prisons is mostly prescriptive, with reduced participation of the prison community, particularly in high security prisons where access to health services is limited by major constraints. Therefore, in a highly endemic prison, we carried out an intervention associating intensive community education and screening at entry in order to assess its feasibility and its impact on case detection.

Population: A high security overcrowded prison for adult males ($n = 785$, 75 inmates/cell, yearly turnover: 80%) followed for one year.

Intervention: 1) At entry, interactive educational sessions and X-ray screening; 2) in the prison, training and supervision of inmate's pair educators, group discussion with inmates (involving TB and ex-TB cases), health workers, guards, psychologists and teachers. TB diagnosed by sputum smear examination and culture in inmates presenting X-ray abnormalities or attending spontaneously the prison dispensary for a cough ⩾3 weeks.

Results: Overall, 62 cases were diagnosed: 29 in response to spontaneous demand and 33 among the 622 inmates (5.3%) screened at entry. TB incidence rate was higher during the intervention compared with the previous year (7898 vs. 4533/100 000, $P < 0.006$). Even though the intervention was well received by inmates, difficulties were encountered in implementing the intervention: frequent transfer of inmates to other prisons, limiting the sustainability of the pair educator program; limitation of inmates meetings and circulation by the administration due to high security regulations; priority given by guards to security and by inmates to survival over health; low motivation of underpaid prison health workers.

Conclusion: The intervention had an important impact on case detection, but insuring its sustainability on the long term under actual conditions would be difficult given security constraints prioritized by the prison administration, and high inmate turnover.

PS-100500-15   Tackling TB in the workplace: experience of working with garment factories in Bangladesh

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Background: The ready-made garment sector in Bangladesh is big and vibrant, employing at least 6 million workers, most of them female. These garment workers are from landless rural families who suffer from high morbidity including from TB. Despite the health care needs of garment workers, provision of health services for them is negligible. This study was an attempt to develop an operational mechanism for an effective and sustainable TB control programme in the garment factories in Bangladesh.

Methods: This operations research was carried out in four areas of Dhaka city, with the NTP, the Bangladesh Garments Manufacturing and Exporting Authority (BGMEA) and three NGOs partners including BRAC. A mapping of garment factories and a baseline survey were carried out to assess the knowledge, attitudes and practices of the management staff and workers on TB care, their willingness to be involved in TB control efforts at the workplace, and on the feasibility of devising a public private partnership (PPP) model for TB control at their workplace. A PPP model was then developed involving all stakeholders under the leadership of the NTP: it is now being implemented and evaluated in 30 garment factories.

Results: The baseline survey suggests that factory managers and garment workers were not aware of the DOTS centres operating near the garment factories, and were reluctant to allow TB patients to seek care during working hours. The medical personnel working in the garment factories also had inadequate knowledge on TB case management. TB patients discontinued their jobs in the factories, left the city and often discontinued TB treatment. Participatory approaches were used to develop tools, protocols and guidelines, and ACSM materials. Training plans for the factory managers and medical personnel were jointly developed and implemented. There have been regular site visits from the NTP, BGMEA, and NGO programme managers using agreed terms of reference.

PS-100643-15   Improving TB medication completion upon being released from prisons in Thailand

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Background: Almost one fifth of TB patients in prisons are released during treatment and have low follow up rates in the community. The objectives are to assess completion of a first visit to the TB clinic within one month of release and to evaluate completion of TB treatment after release.

Methods: An operational research project was performed at five prisons in Thailand. Inclusion criteria were i) Treatment category I or II patients registered from October 2008 to January 2009 ii) remand prisoners or known release schedule prisoners during treatment. Before the release, the patients were provided counseling in the prison by Discharge Planners from a faith based organization. The prison nurses informed the Discharge Planners when the patient was released. Financial assistance for transportation, emergency houses, and medical appointment arrangements were offered. Descriptive data was summarized.

Results: Out of the 29 enrolled patients, 90% (26/29) were released. About 77% (20/26) went to the TB clinic for a first visit within one month of release. The treatment completion among those who made a first visit to clinic was 63% (15/24). Two released patients could not be evaluated because their regimen had been changed to 18 months.

Conclusion: Over three quarters of the released patients followed up at the TB clinic. The large proportion might be due to the relationship between patients and discharge planners. Identifying factors related to those who did not complete either the first visit or the treatment would help improve the prison TB control.

PS-101027-15   Is there a need for tuberculosis screening for health care workers in a low prevalence country?

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Background: Queensland has a low incidence of tuberculosis (TB) ($<4/100\,000$ population/year) with nearly 80% of cases diagnosed between 2002–2009 being overseas born. TB is thus uncommon in many health care settings. This review of health care workers (HCW) screening was undertaken following (a) several large contact investigations following diagnosis of TB in overseas born HCWs, (b) recognition that migrant settlement patterns are changing and (c) recent increased recruitment of HCWs from overseas.

Methods: Retrospective review of all TB cases notified in Queensland 2002–2009 to identify HCWs. The identification of these patients and description of their characteristics were facilitated by prospective collection of relevant data using structured nurse interview forms.

Results: Sixty-six cases were identified of which 42 (64%) had pulmonary TB (15; 23% sputum smear positive), resulting in 10 large contact screening investigations. Molecular epidemiological typing used to identify transmission showed that one case was acquired from an undiagnosed hospital inpatient, two Australian-born retired HCWs with matching types both served in the Australia defence force in the 1950s, three Filipino born had matching types with no link established and two overseas born doctors matched but link not established. Risk factors for the Australian-born showed previous travel or residence in high risk countries, known TB contact and previous service in the defence forces.

HCW	Medical officer	Nurse	Allied health worker/ cleaner	Total
Total	22	24	20	66
Male	15	3	8	26
Female	7	21	12	40
Currently working	19	18	16	53
Retired	3	6	4	13
Presented with symptoms	14	13	16	43
Active screening	4	8	3	15
Incidental diagnosis	4	3	1	8
Australian-born	1	3	7	11
Overseas-born	21	21	13	55
LRC	4	4	2	10
HRC	17	17	11	45
Worked or travelled in HRC*	11	7	4	22
Known close contact with patient in community	10	11	6	27
Close contact with TB patient in health care setting in Australia since 2000	0	5	1	6
Close contact with TB patient in health care setting overseas	10	6	5	21
Close contact with patient in community—possible				6
Close contact with patient in community—not stated				33

* Australian- and LRC-born patients only.
LRC = low risk country (TB incidence < 50/100 000 pop); HRC = high risk country (TB incidence ≥ 50/100 000 pop).

Conclusions and recommendations: Despite low incidence of TB in the community in Queensland, TB continues to be diagnosed in HCWs. Eighty three percent of TB in HCWs were foreign-born; thus awareness needs to be maintained in health care settings and there is need to strengthen and maintain a standardized statewide TB screening. It is essential to continually review the incidence of TB in HCWs and the current risk for transmission in Queensland health settings to inform the need and extent of TB HCW screening.

PS-101368-15   New challenges to controlling tuberculosis in hard-to-reach populations— can we work alone?

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Background: In London, 1 in 6 tuberculosis (TB) cases are hard-to-reach due to homelessness, drug/alcohol use or imprisonment. These populations suffer disproportionate co-morbidity with blood borne virus infections (HIV, HBV, HBC). Find&Treat, a multidisciplinary pan-London specialist outreach service, screen over 8,000 people annually with mobile chest radiography and detect a rate of 264 per 100 000 (PPV 0.22). Find&Treat supports case-managements for over 400 active TB cases with complex social problems and locates and returns over 50 lost to follow up cases to treatment each year. Despite the intervention being cost-effective and potentially cost-saving, sustaining funding is challenging.

Methods: We undertook a service mapping exercise of allied providers who work with hard-to-reach groups to identify opportunities to integrate screening, care pathways and case management activities more effectively and efficiently. We then piloted a combined screening intervention in a homeless hostel that supports problematic drug users.

Results: Across London we identified 223 front-line allied services who work with hard-to-reach groups including 84 hostels serving a population of more than 3000 homeless people, 56 day centres and 83 community drug and alcohol projects. All these services represent potential points of collaborative care for outreached screening initiatives. The hostel pilot demonstrated multiple testing as acceptable and convenient to the client group, 51/53 (96%) accepted TB screening of who 34/53 (64%) also accepted HIV, HVB and HVC testing.

Conclusion: TB screening and case-management services for hard-to-reach populations are resource intensive and may be more operationally and cost-effective when combined with initiatives for other prevalent infections.

PS-100834-15 Approaches to overcoming TB and HIV/AIDS epidemic among IDUs in Cherkassy region of Ukraine

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Background: In Cherkassy region there is a steady growth of HIV/AIDS and tuberculosis epidemics mostly among injection drug users. In 2008, 708 persons had TB, 82 of them were diagnosed TB in conjunction with AIDS for the first time. There were 357 persons with HIV infection in 2008, including IDUs—134. Estimated number of IDUs in the region —11000 persons.
Methods: In the region there is an established collaboration between 8 HIV-service regional NGOs, TB dispensaries and AIDS centers. On the basis of TB dispensaries IDUs with TB receive HIV prophylactic services package—syringes, condoms, alcohol wipes, IEM, social worker counseling, rapid testing for HIV and syphilis. There is a referral system to redirect IDUs from stationary and street syringe exchange points (SEP) to TB dispensaries and to AIDS Centers for consultation, diagnostics and timely treatment with social support. In order to approach medical care to IDUs phthisiatricians, infectionists are providing consultations on the basis of HIV-service NGOs (community centers, stationary SEP), a mobile clinic that functions as mobile SEP.
Results: In frames of projects of harm reduction, presented models of HIV prevention among IDUs with TB and timely detection and treatment of tuberculosis among IDUs are new for the country. On the basis of TB dispensaries for 2008–2009, prevention services for HIV infection were provided for 286 IDUs with TB. In 2009 in the harm reduction program phthisiatricians provided IDUs with about 900 consultations, infectionists—with 1440.
Conclusions: The success in overcoming the two epidemics is possible if using comprehensive measures and coordination at regional level. Cherkassy experience can be spread to other Ukrainian regions.

TB-HIV CLINICAL RESEARCH AND CARE: DIAGNOSIS/TREATMENT OUTCOMES/ CLINICAL MANAGEMENT

PS-100728-15 Express diagnostics of multidrug resistance of *M. tuberculosis* from patients with TB-HIV co-infection

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Early diagnosis of TB and rapid testing of rifampin (R) and isoniazid (H) resistance are important to efficient treatment and control of drug-resistant (MR) TB. The purpose of the research was studying of clinical and diagnostic importance of molecular-genetic methods as TB-biochip in 124 HIV positive patients with clinical and radiological signs of TB and negative results of clinical material (CM) bacterioscopy for asid-fast mycobacteria. CM: sputum, bronchoalveolar lavage liquid, blood, body fluid, lymph nodes. DNA was isolated with the help of commercial set. TB-biochip can simultaneously identify mutations in four MBT genes associated with MR to (R) and (H): *rpo*B, *kat*G, *inh*A, *ahp*C. Mutations in *rpo*B gene were revealed in 82 (66.1%) cases. Thus the replacement of codon 531 in 41 (50.0%), including (Ser531-Leu) in 35.4%. This mutation is mostly distributed among R resistance strains in the world and commonly connected to Beijing genotype. This replacement causes MR to high concentration R in vitro and does not affect MBT viability. Replacements in other codons: 511 (11), 512 (7), 516 (8), 513 (6), 526 (5) and 533 (4) cases. MR to H, caused by mutations in *kat*G gene, was revealed in 68 (54.8%) cases. The prevalence of the strains with the combination of mutations of *rpo*B531 and *kat*G315 once again confirms the presence of pool of MR strains of Beijing genotype at territory of North-West region of Russia in conditions of wide application of R and H. We have revealed the replacement of nucleotides of inhA gene in 28 (22.5%) patients. The ahpC gene has lowest number of mutations—7 (5.6%). This the method of TB-biochip is high sensitive and specific for express (48 hours) detection of MR MT.

PS-100217-15 Integrating TB screening tool in clinical records improves TB detection in HIV/AIDS patients in TASO

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Background: Globally 9.2 million new TB cases and 1.6 million deaths occur annually, 16% of new TB patients are HIV positive (WHO, 2007), Uganda estimated 70% of TB cases are HIV positive (NTLP, 2007). In 2008 out of 82114 (94%) of TASO registered clients screened for TB, 1960 (2.4%) were diagnosed with TB and treated (TASO MIS). Globally case target detection target is 70% of infectious TB and successfully treat 85%. Uganda detection rate is 60.1%, cure rate 62.2 % (HSSP II), integrating TB screening tool reminded clinicians to screen for active TB in TASO.

Methodology: This involves prompt triaging and completing clinical record forms by assessing if the patient enrolled for TASO care is symptomatic for TB using a screening tool. Patients who screened positive for one or more signs/symptoms were further investigated to confirm active TB by sputum analysis, chest X-ray, lymph node aspirates and pleural tap for analysis. Cases with confirmed TB received respective treatment as they continue to attend the usual medical review on appointment.

Results: Overall percentage of patients screened for TB improved from 78% to 90% between fourth quarter, 2008 and first quarter, 2009. Of those screened the percentage of patients with at least one or more positive signs/symptoms increased from 23.3% to 42.5% within the same period TASO Tororo MIS, out of those with a positive screen who took a test, the percentage of patients diagnosed with TB increased from (26/126) 15.9% to (38/141) 27% within the same period.

Conclusion/recommendation: Integrating screening tool in clinical record will; prompt clinicians to screen for active TB at each clinic visit, allow continuity and quality of TB care, prevent unmasking of TB through immune reconstitution syndrome in patients with lower CD4 cell count initiating ART and monitors TB investigation results, treatment, progress and outcome.

PS-100564-15 Patient drop-out from tuberculosis diagnosis in HIV-infected adult Ugandans

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Background: Examination of two sputum samples by smear microscopy is the standard and only widely available test for diagnosis of pulmonary tuberculosis in high burden countries. After submitting a 'spot' specimen at the initial visit, some patients fail to return the following day to submit the second, 'early morning' specimen, a phenomenon called diagnostic 'drop-out.' We sought to identify factors associated with patient drop-out and to estimate how many possible smear-positive patients were not diagnosed because of drop-out.

Methods: We conducted a retrospective study among patients attending an HIV clinic in Kampala, Uganda, with cough ⩾2 weeks between September 2008 and March 2009. We collected sputum smear microscopy results from the laboratory register and demographic and clinical data from the patient's medical record.

Results: Of 600 TB suspects, 86 (15%) were diagnosed with smear-positive TB. 68 (79%) were diagnosed on the first sputum sample, and 18 (24%) on the second (Figure), while 193 patients never returned for their second sputum. Drop-out was not associated with sex, age, ART, CD4-count, cough duration, distance traveled, employment, or income. Assuming the proportion of smear-positive patients was similar among those who did and did not return, we estimate that we failed to identify about 10 (10%) smear-positive TB patients because of drop-out.
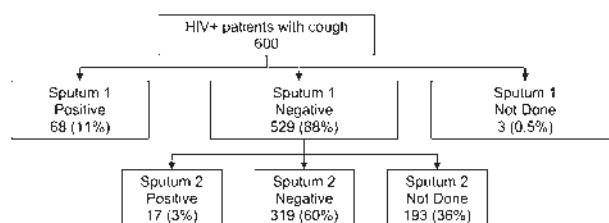

Figure Diagnostic outcomes of 600 TB suspected patients at an outpatient HIV/AIDS clinic at Mulago Hospital, Kampala, Uganda.

Conclusions: Drop-out during the diagnostic process is extremely high, even among patients attending a well-resourced HIV-clinic. Collecting and examining second sputum while the patient is in the clinic, rather than the following morning, could increase case detection.

PS-100631-15 *M. avium* complex is uncommon among AIDS patients in a setting with high prevalence of TB

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Aim: To detect the hospital based prevalence of infection by *M. avium* complex (MAC) among AIDS patients with high clinical suspicion in Peru.

Methods: The study was carried-out in the Cayetano Heredia Hospital in Peru, from February to December 2006. Consecutive AIDS patients with a clinical suspicion of infection by micobacteria and <100 CD4+ cell/µl were recruited. At least a 5 ml sample of blood was collected and cultured in automated system using Myco-F-Lytic media (BD diagnosis). Additional samples for detecting active tuberculosis and MAC infection were processed using the same media and MGIT and Löwenstein-Jensen medium based on clinicians' request. All positive isolations for acid-fast bacillus (AFB) were typified by PCR of the IS6110 region and 16S rRNA sequencing.

Results: 47 patients were enrolled; median age was 34 years (range 21–50); 34 (72%) were male; median CD4+ cells count was 38 (range 2–96); 81% had consumption; 74% had fever; 60% had diarrhea and 60% had cough. 22 AFB were isolated from 12 patients: 8 in blood, 4 in lung samples, 3 in CSF, 3 in bone marrow and one in pericardial fluid, hepatic abscess and duodenal abscess. All isolates were *M. tuberculosis* according to molecular assays; 34 (72%) started TB treatment and 19 (41.3%) out of 46 patients died during the following year; 6 (50%) of the 12 TB culture positive patients died.

Conclusion: MAC was uncommon in patients with AIDS and low CD4+ cells count in Peru. TB continues to be the most important mycobacterial disease in AIDS patients in highly prevalent settings. Early diagnosis and treatment of HIV and TB are necessary due to the high associated mortality of this co-infection.

PS-100700-15   Evaluation of nurse-led diagnosis of smear-negative tuberculosis using point-of-care C-reactive protein

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Background: WHO guidelines recommend that HIV-positive smear-negative tuberculosis (SNTB) suspects are evaluated by a physician, including clinical examination and chest radiograph. This is difficult to implement in resource limited settings. C-reactive protein (CRP) levels are raised in HIV-associated tuberculosis. We evaluated the interim outcomes of nurse-led diagnosis of smear-negative pulmonary tuberculosis using a point-of-care CRP assay.

Methods: In this ongoing study HIV-positive smear-negative tuberculosis suspects with cough for >2 weeks referred from primary-care clinics were recruited in the outpatients department of Edendale Hospital in KwaZulu-Natal, South Africa. All participants received a five day course of broad-spectrum antibiotic before evaluation. Nurse researchers reviewed participant symptoms and point of care CRP (NycoCard CRP Reader II, Axis-Shield, Norway), and made a diagnosis of either smear-negative tuberculosis or not tuberculosis. Participants were then reviewed by an expert physician using WHO guidelines. The physician was blinded to the nurse's diagnosis and CRP result. Induced sputum was sent for mycobacterial culture.

Results: Evaluation was complete in 42 participants with median CD4 count 189 cells/microlitre (IQR 67–270). Culture positive tuberculosis was confirmed in 18 participants, of whom 12 (67%) were diagnosed by the nurse-researchers and 15 (83%) by the physicians. Overall, the physicians diagnosed 22 cases and the nurses 29 cases of SNTB: 15 (68%) of the physician-diagnosed cases were also diagnosed by the nurse-researchers.

Conclusion: Nurse-based diagnosis of SNTB using point-of-care CRP may of use in resource-limited settings. Further data will be presented.

PS-101097-15   Assessment of microscopy and culture techniques in the diagnosis of TB amongst HIV patients

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Background: The diagnosis of active TB in HIV infected patients continues to be a great challenge especially when their HIV infection is advanced. Culture for acid-fast bacilli (AFB) is the gold standard and much more sensitive than microscopy which has been the mainstay of TB Control Programme. However, it is not readily available in most of the laboratories due to cost and infrastructure requirements. In this study, we assessed the yield of AFB by microscopy and culture for active TB diagnosis in HIV patients.

Methods: 1477 HIV patients were screened for AFB by microscopy and culture using NALC-NaOH method at the National TB Reference Laboratory, Lagos, Nigeria from 2008 to 2009. Information on HIV status of each patient was obtained from their medical records. Ziehl-Neelsen (ZN) stained smears were made from the final deposits and examined under light microscopy for AFB. Loopfuls of each of the final deposits were evenly spread on the entire surface of Löwenstein-Jensen slopes and incubated at 370C. The slopes were examined for growth on day 3, 7 and weekly thereafter for 8 weeks. Slopes with growths, smears of colonies were made, stained by ZN and examined for the presence of AFB.

Results: Of the 1477 patients, 480 were AFB positive.

230 (15.6%) were detected by culture, 125 (8.5%) were detected by microscopy while 125 (8.5%) were detected by both methods. The difference between the detection for culture and microscopy was statistically significant, $P < 0.05$.

Conclusion: The higher yield of AFB by culture compared to microscopy confirms the higher sensitivity of culture for active case finding of TB in HIV patients. There is therefore an urgent need for the Nigeria and other resource countries to increase capacity for culture facilities in TB laboratories.

PS-100811-15 *Mycobacterium tuberculosis bacteremia and mortality in Ugandan patients with severe sepsis*

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Aim: Autopsy studies from sub-Saharan Africa reveal a high frequency of undiagnosed disseminated *Mycobacterium tuberculosis* infection in HIV-infected patients. Several studies also report a high prevalence of *M. tuberculosis* bacteremia, a form of disseminated tuberculosis. The clinical presentation of *M. tuberculosis* bacteremia mimics other blood stream infections making it difficult to properly identify and treat. We report the prevalence and outcomes of patients with *M. tuberculosis* bacteremia in a cohort of severely septic Ugandan patients.

Methods: From May 2008 to May 2009, we prospectively enrolled 427 patients from two Ugandan hospitals based on established criteria for severe sepsis. Laboratory testing included HIV serology, CD4 cell count and aerobic and mycobacterial blood cultures. After detection with a BACTEC 9120 instrument, mycobacteria were grown on solid culture media and identified as *M. tuberculosis* complex with PCR amplification. The primary outcome was 30-day mortality.

Results: *M. tuberculosis* bacteremia occurred in 86 (20.1%) of 427 patients; cultures, on average, took 19 days to grow. All 86 patients were HIV-infected-median CD4 count (cells/mm³) was significantly lower in patients with *M. tuberculosis* bacteremia than patients without *M. tuberculosis* bacteremia (17 vs. 63.5, $P < 0.001$). Patients with *M. tuberculosis* bacteremia had a significantly increased 30-day mortality compared to patients with positive aerobic and negative

blood cultures (Figure). The primary medical team infrequently evaluated these patients for *M. tuberculosis* infection, having obtained AFB sputum on only 30% and chest X-rays on ~50% of patients.
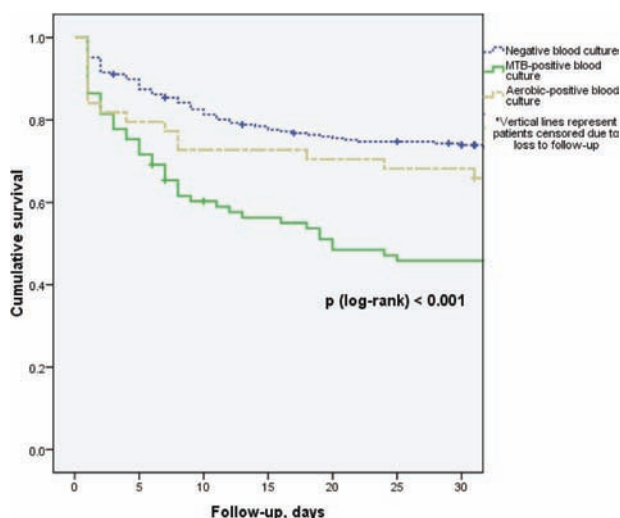

Figure Survival with respect to blood culture results in patients with severe sepsis.

Conclusion: One in 5 patients hospitalized with sepsis syndromes in 2 Ugandan hospitals have *M. tuberculosis* bacteremia and HIV coinfection with severe immune suppression. Mortality in these patients is significantly higher than those with positive aerobic or negative cultures. Clinical suspicion for *M. tuberculosis* sepsis in critically ill patients is low among health providers. Diagnostic tests which identify *M. tuberculosis* sepsis early are needed.

PS-100999-15   Derivation of a clinical decision rule using C reactive protein to rule out SNTB in a high prevalence population

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Background: Measurement of C reactive protein (CRP) as part of a clinical predication rule may expedite assessment of smear-negative tuberculosis suspects in high HIV prevalence settings.

Methods: A multiple regression logistics regression model was constructed using history, physical exam, imaging and laboratory exams to predict the diagnosis of SNTB using data from a prospective study of sputum smear-negative tuberculosis suspects in KwaZulu-Natal, South Africa.

Results: A multiple regression model determined that having sweats (OR 2.3, 1.3–3.9, $P = 0.003$) and

a higher C reactive protein (CRP) on admission (OR 1.006, 1.002–1.009, $P = 0.006$) were significant risk factors for TB and patients who received previous antibiotics (OR 0.48, 0.29–0.81, $P = 0.006$), had a higher hemoglobin (OR 0.86, 0.77–0.95, $P = 0.005$) and Karnofsky score (OR 0.96, 0.94–0.98, $P = 0.001$) were less likely of having TB. We identified 127 patients categorized as low risk for having TB (probability <20%) using our regression model. Using a CRP cut point of ⩽10 mg/L, 73 (73/421 or 17%) patients could have been sent home safely with no further follow up using the clinical decision rule. The model had a 100% sensitivity and negative predictive value with no false negative results.

Conclusions: CRP may play an important role in ruling out SNTB in low risk TB suspects in an outpatient high HIV prevalence setting. Reducing the number of patients that require the costly and labour intensive work up associated with SNTB cases would allow for more efficient allocation of resources. Prospective validation of the model is needed.

PS-101005-15 TB treatment outcomes before and during collaborative TB-HIV activities in Bulawayo, Zimbabwe

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Background: Measures to reduce HIV burden in tuberculosis (TB) patients were integrated into primary health care services at two Bulawayo city clinics which provide TB diagnostic and treatment services and were accredited to start co-infected patients on antiretroviral therapy in August–September 2008. The objective of this study was to ascertain whether introduction of HIV-related services influenced TB treatment outcomes.

Method: TB treatment outcomes for new smear-positive patients registered at the pilot sites between 1 January 2007 and 31 March 2009 were analysed using the pilot site TB registers that were entered into an Epi Info (version 3.5.1.) database.

Results: A total of 334 new smear-positive patients (85% were HIV-infected) were registered at Emakhandeni and Magwegwe Clinics in the study period and all were evaluated. As shown in table below, the success rates ranged from 70% to 81%. Most patients with unfavourable TB treatment outcomes (range 20% to 30%) died (range 9% to 20%) and default among patients remained infrequent (range 0% to 7%).

Conclusion and recommendations: Introduction of joint TB-HIV services in a setting with heavy work load, limited resources and a high HIV prevalence among TB patients did not deter TB treatment outcomes at the pilot sites where success rates above the national average (60%, 2006) were attained. High mortality among TB patients was observed and it is anticipated that HIV diagnosis and care now readily available through 'one-stop shop' service will decrease deaths among co-infected patients.

Year	No new PTB+ registered and evaluated	No (%) cured	No (%) treatment completed	No (%) success	No (%) died	No (%) defaulted	No (%) transferred out
			Emakhandeni Clinic				
2007	62	42 (68)	8 (13)	50 (81)	10 (16)	1 (2)	1 (2)
2008	42	30 (71)	0	30 (71)	7 (17)	3 (7)	2 (5)
2009 (Q1)	10	8 (80)	0	8 (80)	2 (20)	0	0
			Magwegwe Clinic				
2007	128	90 (70)	6 (5)	96 (75)	12 (9)	3 (2)	17 (13)
2008	76	48 (63)	5 (7)	53 (70)	15 (20)	0	8 (10)
2009 (Q1)	16	12 (75)	0	12 (75)	3 (19)	0	1 (6)

PS-101185-15 Reducing mortality in smear-negative pulmonary tuberculosis HIV-infected patients, KZN, South Africa

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Background: In 2006 the World Health Organization (WHO) released revised guidelines for the diagnosis and treatment for HIV-positive, smear-negative TB suspects. For resource-limited countries where microscopy remains an inadequate diagnostic tool, an algorithm was proposed to reduce morbidity and mortality in those seriously-ill. We sought to evaluate the guidelines' diagnostic utility in an algorithm cohort compared to observed standard practice in patients admitted to three hospitals in KwaZulu-Natal, South Africa.

Methods: We conducted a prospective observational study before and after algorithm implementation. We assessed hospitalization status at 7 days, TB treatment status, and 8-week post-admission mortality. Inclusion criteria were age >5 years, HIV-infection, signs of being clinically seriously-ill, cough >2 weeks, radiographic abnormalities consistent with TB, and at least two negative sputum smears. A one week trial of antibiotics was allowed in the standard treatment cohort; concomitant antibiotics in the algorithm.

Results: We screened 871 seriously-ill patients and enrolled 351 HIV-infected TB suspects for the standard practice cohort, and 992 seriously-ill patients and 187 TB suspects for the algorithm cohort. Seven days after admission, 27% (50/187) of algorithm patients were still hospitalized, compared to 37% (131/351) of standard practice patients (Risk ratio [RR] 0.72,

95% Confidence Interval [CI] 0.55–0.94). There was no significant difference in the proportion on antiretrovirals, 17% versus 15%, respectively ($P = 0.48$). Eight weeks after admission, 83% (156/187) of algorithm patients were still alive, compared to 68% (239/351) of standard practice patients (RR 1.23, 95%CI 1.11–1.35). Only 47% of the standard practice patients were given anti-tuberculosis treatment.

Conclusion: Implementation of the WHO algorithm has the potential to drastically reduce mortality in seriously-ill, HIV-infected, sputum smear-negative TB suspects in RSA.

PS-101223-15   Tuberculosis and HIV co-infection in a five-year-old girl

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Background: In adults co-infected with HIV and tuberculosis (TB), initiation of highly active antiretroviral therapy (HAART) during TB therapy significantly improved survival despite a higher incidence of immune reconstitution inflammatory syndrome (IRIS) compared to sequential therapies (1).

Case report: A five-year-old girl born in Kenia was admitted to the ICU with life threatening pneumonia. She had a history of TB, treated at the age of 3. At admission, TB skin test and interferon gamma release assays (IGRAs) were negative. HIV-antibodies were positive, the CD4 cell count was low (138/µl), the viral load was high (397.000 copies/ml). Bronchoalveolar lavage revealed acid-fast bacilli, subsequent PCR and culture identified full drug-sensitive *M. tuberculosis*. An antituberculotic regimen was initiated urgently (Isoniazid, Rifampicin, Pyrazinamid, Ethambutol). After 14 days HAART (Abacavir, Lamivudin, Nevirapin) was started. The girl improved rapidly but developed severe IRIS 18 days after initiation of HAART. IRIS was treated successfully with prednisolone. TB therapy was terminated after 9 months.

Conclusions:

1 In countries with low incidence of both TB and HIV, awareness for co-infections should be high in severely sick patients particularly in immigrants from high-prevalence countries.

2 Negative TB skin tests and/or IGRAs in HIV+ patients with low CD4 counts do not exclude TB.

3 Our treatment regimen and the clinical course is in accordance with study results in co-infected adults showing increased occurrence of IRIS but less mortality in patients receiving HAART during TB therapy compared to those receiving sequential therapies (1).

1 NEJM 362: 697; 2010.

PS-101544-15   Pandemic Influenza A (H1N1) outbreak in 15 HIV-infected children

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Background: For patients infected with the human immunodeficiency virus type 1 (HIV-1), the clinical course and overall health risk after 2009 H1N1 influenza virus infection is not well established.

Objective: We describe the clinical course, kinetics of viral shedding, and the H1N1 influenza-specific humoral immune response among HIV-infected children.

Design: Observational study after an outbreak of 2009 H1N1 influenza virus infections among a travel group of 15 HIV-infected children (aged 8.9–16.8 years) in Germany in October 2009. All children had been treated with highly active antiretroviral therapy and had CD4 cell counts exceeding 350/µL. Disease symptoms were recorded and shedding of H1N1 influenza virus was assessed by detection of virus-specific RNA and culture of virus from nasal secretions. Serum levels of H1N1-specific antibodies were determined at 6 weeks after symptom-onset.

Results: In all 15 children of the travel group, infection with the 2009 H1N1 influenza virus was confirmed by viral culture and reverse transcriptase polymerase chain reaction from nasal secretions ($n = 11$) and/or detection of 2009 H1N1-specific antibodies. Fourteen children (93%) had symptoms of disease, mostly consisting of low-grade fevers and cough. Five children (33%) had high grade fevers (>39°C) and, thus, were treated with oseltamivir. Among the 11 children in whom viral shedding was assessed, viral RNA was detected for 4 versus 8 days ($P = 0.005$), and cell cultures tested positive for 3 versus 6 days ($P = 0.005$), respectively, among oseltamivir-treated ($n = 5$) and non-treated ($n = 6$) children. At 6 weeks after symptoms-onset, all children had developed H1N1 virus specific antibodies.

Conclusions: Clinical course, kinetics of viral shedding, and rate of emergence of virus-specific antibodies among school-aged HIV-infected children with 2009 H1N1 influenza virus co-infection did not appear to be different from those described for healthy children.

PS-101000-15   Early mortality in HIV-infected patients undergoing treatment for smear-positive pulmonary TB

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Background: In sub-Saharan Africa, case fatality rates in tuberculosis patients have risen enormously in the last few decades and have been associated with HIV infection. A substantial proportion of these deaths occurs early in the course of treatment.
Objectives: To determine the early mortality rate and identify simple determinants of early deaths (defined as death within the first 8 weeks of treatment) in HIV infected patients undergoing treatment for new smear positive pulmonary tuberculosis in Yaoundé, Cameroon.
Design: A prospective cohort study of all new patients aged 15 years and above with smear positive PTB.
Setting: Tuberculosis centre of Hôpital Jamot, the main referral and tuberculosis treatment facility for Yaoundé and its surrounding areas.
Main outcome measures: Death and survival during the 2 month intensive phase of treatment in hospital.
Results: A total of 501 new patients with smear positive pulmonary tuberculosis were hospitalized over the study period. Of these, 160 (31.9%) were HIV positive. Of the 160 HIV coinfected patients, 81 (50.6%) were male and 79 (49.4%) were female with a mean age of 36.41 years (range: 18–67 years). Nineteen of the 160 HIV-infected patients eventually died during the two month intensive phase of treatment giving an early mortality rate of 11.8% (95%CI: 6.8–16.8). Logistic regression analysis showed that age above or equal to 40 years (OR = 4.96; 95%CI: 1.73–14.25; P = 0.0029) and a CD4 cell count less than or equal to 200/mm³ (OR = 4.99; 95%CI: 1.32–18.77; P = 0.0174) were significantly and independently associated with early in hospital death of HIV positive patients with smear positive pulmonary tuberculosis.
Conclusion: In Yaoundé, Cameroon, the early in-hospital mortality rate in HIV infected patients undergoing treatment for new smear positive pulmonary tuberculosis is relatively high.

PS-100515-15   Combined mobile testing for HIV and TB can provide high quality services for hard-to-reach populations

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Background and objectives: A major challenge for the introduction of novel interventions is their roll-out into rural areas. The dual burden of HIV and TB makes an integrated approach inevitable. Therapy of both diseases is often obstructed by delayed diagnosis. However, current technologies are either not sensitive enough (microscopy) or technically too challenging to be implemented in point of care facilities. The presented pilot study evaluates the feasibility of a Mobile Diagnostic and Training Centre (MDTC) to provide hard to reach populations with access to high quality HIV-TB diagnosis and staging
Methodology: A community randomized controlled study evaluates the effect of regular 3-monthly visits through the MDTC on TB-notification numbers in the respective communities. In addition, data on immune status at time of diagnosis, survival during TB treatment and acceptance of services are collected. Three strata with 8 health facilities each (1: regular MDTC visits, 2: infrastructural and training support only and 3: no support) are compared before intervention and one year after. The MDTC is equipped with modern technology, including fluorescence smear microscopy, a GeneXpertTB real time PCR (from Q3 2010), a Guava flow cytometer, a Sysmex cell-counter and a Reflotron clinical chemistry analyser
Results: Initial results after 3 months indicate that the project is technically feasible and well accepted in the population. On average 27 patients are receiving HIV services and 9 patients TB screening daily. So far 13% of patients were HIV positive, 4% could be diagnosed for TB with a positive smear. Analysis of a small subset of 100 frozen sputum samples by GeneXpert assay showed that this rate can be doubled with a more sensitive technique
Conclusions: We are confident that the MDTC is an operationally feasible tool to bridge the time until simpler and wider applicable diagnostic methods allow sensitive and rapid TB diagnosis and HIV staging in underserved areas.

PS-100468-15   Missed opportunities for diagnosis of TB and HIV co-infection in the Lesotho apparel industry

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Background: The Lesotho apparel industry is ravaged by the high 41% HIV prevalence. Opportunities to diagnose HIV among TB patients are often missed due to separate and often vertical TB and HIV program in the public and private settings. A review on the uptake of provider initiated HIV Testing and Counselling (HTC) among Lesotho apparel is being reported.
Intervention: The Apparel Lesotho Alliance to Fight AIDS (ALAFA) program is a comprehensive HIV and AIDS workplace based industry wide program providing HIV prevention and treatment for HIV and related conditions for a 42 000 workforce. In line with the government policy ALAFA advocates for HIV testing among TB patients or patients with TB related symptoms like weight loss, fever, night sweats or haemoptysis within the workplace and TB testing for all HIV infected workers. TB-HIV integration activities also include building capacity among service providers to manage the two conditions in the same clinic.
Results and lesson learnt: Overall 6450 HIV infected apparel workers are enrolled in the program. 212 apparel workers were being treated for tuberculosis in 2009. 198 of the TB patients now know their HIV status and 97% are HIV infected. 67% of TB patients whose the HIV status is known, HIV diagnosis preceded TB diagnosis at the workplace clinics and 32.3% tested for HIV after referral for directly observed therapy at the workplace clinics from the public clinics. All TB and HIV co-infected patients have been initiated on ART. Acceptance of HCT is high, only 14 patients referred so far have declined the HIV test.
Conclusion and recommendations: Opportunities for HIV testing among apparel workers co-infected with TB and HIV may be missed both at the workplace clinics and the public facilities. There is an urgent need for increased staff capacity building in the private sector for management of TB and HIV co-infection, full integration and coordination of the TB and HIV care services at the workplace clinic.

PS-100609-15   HIV rapid test for tuberculosis patients: implementing referral centers in Rio de Janeiro TB clinics

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Introduction: Rio de Janeiro City has a high tuberculosis (TB) incidence rate (97/100 000). In 2007, 6882 TB cases were reported, 11% of which were HIV positive. Despite the fact that the Brazilian Guidelines recommends that every TB case should be tested for HIV, only 45% of the 2007 TB patients cohort were tested. ELISA is the standard method of screening test for HIV antibody performed in Brazil but, because of logistics problems, it can take a long time for the Health Units to have access to the results. In March 2008, the city Health Department, in collaboration with the Global Fund, had begun the implementation of seven Referral Diagnostic Centers for HIV using Rapid Tests for TB patients.
Aim: The aim of this report is to describe the implementation process of these Referral Centers and demonstrate how expanding access to HIV serological diagnosis favors early detection of TB-HIV co-infection.
Methods: Seven Referral Centers for HIV Rapid Test were implemented in TB clinics from March 2008 to September 2009. 88 health professionals were trained on how to perform HIV Rapid Test and 179 health professionals who assist TB patients were trained in HIV counseling. Although ELISA continues to be the routine test, HIV Rapid Test is performed when ELISA results are not available at the end of the second month of TB treatment.
Results: From March 2008 to December 2009, 501 TB patients knew their HIV status using HIV Rapid Test at the TB Referral Centers, from which 45 (9%) had a positive result (Table).

# TB patients sent to perform Rapid Test	#TB patients who performed the test	Sex		Mode of treatment		Reasons for the Rapid Test request				
		Masc	Fem	DOT	No DOT	ELISA not available (end of the 2nd mo TB treatment)	Worsening clinical condition	Others	Test positive	
573	501 (87%)	329 (66%)	184 (37%)	315 (63%)	186 (37%)	276 (55%)	16 (3.2%)	209 (42%)	45 (9%)	

Conclusion: The use of HIV Rapid tests for TB patients can be a useful tool to increase diagnosis of HIV by reducing barriers of access to perform the exam. This fact facilitates early opportunity to initiate treatment and to implement prevention activities.

PS-100976-15   TB screening in Prevention of Mother-to-Child Transmission and antenatal care settings

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Issues: In generalized epidemic settings, HIV-related illness is significant cause of maternal morbidity and mortality. In such settings, the integration of key HIV interventions in routine Maternal and Child Health (MCH) services is important. The routine screening of HIV-positive women for TB is one of such interven-

tions. TB during pregnancy and postpartum period poses serious challenge to the well-being of women and their infants.

Description: Integrated Management of Adolescent and Adult Illness (IMAI)/ Integrated Management of Pregnancy and Childbirth (IMPAC) provides training tools and job aids for health workers to integrate HIV prevention, care, treatment and ART, including routine screening of HIV-positive pregnant women for Tuberculosis (TB) during each facility visit, in Antenatal Care (ANC) settings. WHO has supported training of health workers, and assisted countries in the adaptation and implementation of these operational tools. Experience of selected countries in screening pregnant women for TB in ANC settings will be presented and discussed.

Lessons learnt: The IMAI/IMPAC clinical course provides guidance for health workers to integrate PMTCT into ANC settings. It helps health workers to recommend HIV testing and counselling, and provide HIV care, treatment and ART for HIV-positive pregnant and postpartum women. Integration of services and health workers ongoing learning after training are important to expand access to key interventions for HIV positive pregnant women.

Conclusion: In high HIV-prevalent settings, reducing the burden of maternal morbidity and mortality calls for comprehensive action that includes addressing obstetrical and HIV-related medical issues. Integrated approach to building health workers capacity minimizes missed opportunities.

PS-101104-15   Eligibility and antiretroviral uptake among newly diagnosed adults HIV-infected TB patients, Kenya

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Background: Nyanza Province contributes 20% of Kenya's TB burden and ~70% of TB patients are HIV co-infected. HIV testing among TB patients exceeds 80%; however antiretroviral therapy (ART) uptake among eligible co-infected patients ranges from 30–50%. We describe ART uptake among adult TB patients newly diagnosed with HIV.

Methods: We conducted a retrospective chart review among TB patients in 50 health facilities providing both TB and ART services. At each clinic we randomly selected 20 ART-eligible TB-HIV patients registered from October 2006 to April 2008. Per Kenya national guidelines, TB-HIV patients were ART-eligible if extra-pulmonary TB (EPTB), pulmonary TB (PTB) and CD4 < 350 or unknown, or PTB and WHO stage 4 disease.

Results: 16 421 TB patients enrolled at these facilities; 9758 (59%) were TB-HIV co-infected. Only 984 (98%) records were abstracted as 5 facilities enrolled <20 eligible patients. 516 (52%) patients were female and the median age was 32 years; 798 (81%) had PTB. Only 335 (34%) had CD4 data available; the median CD4 cell count was 130 cells/mm³. The majority, 533 (54%) had PTB and CD4 unknown, followed by 260 (26%) with PTB and CD4 < 350; 186 (18%) had EPTB, and 5 (1%) had PTB with CD4 ⩾ 350 but were WHO stage 4. ART was started in 439 (45%) during TB treatment, only 247 (25%) had a known date of ART initiation. The median timing of ART initiation from TB treatment start was 3 months (range 0–29 months). Patients with PTB and CD4 < 350 were more likely to have started ART, 208 (80%) compared to EPTB 97 (52%), PTB and CD4 unknown 132 (25%), and PTB with CD4 count ⩾ 350 and WHO stage IV 2 (40%); $P < 0.001$ for all comparisons.

Conclusion: Over 50% of TB patients were HIV co-infected; ART uptake among eligible patients was 45%. 80% of eligible TB patients had PTB, and PTB patients with CD4 data were most likely to initiate ART. There is a need to improve CD4 access among TB patients and provide better linkages and documentation of ART uptake.

PS-101133-15   Importance of when TB screening questions are asked on intake sheet in VCT

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Background and implementation approach: Botswana has a TB prevalence rate of 454/100 000 persons (WHO) and is actively fighting the dual pandemics of TB and HIV. Tebelopele VCT is the largest NGO provider of HIV counseling and testing services and provided over 150 000 tests in 2009. In September 2008, Tebelopele began using TB screening questions for all clients who tested for HIV and referring symptomatic respondents for further TB screening and treatment.

Analysis and design method: Qualitative data was collected from focus group discussions with Tebelopele counselors, and CT session observations. The focus group discussions were semi-structured, and held in eight of Tebelopele's sixteen centers. The number of sessions observed ranged from one to four at each center.

Results: During the focus groups, counselors were concerned about CT session length and rarely ask every question on the form. Instead, they rely on the discussion to infer how the questions should be answered and rarely ask clients TB screening questions.

In total, 20 CT sessions were observed after counselors first asked clients within the privacy of a counseling room for consent for the session was observed. It was found that TB screening questions were asked in less than 25% of observed sessions, which is consistent with the length of time the counselor spent on support during the CT session.

Conclusions and recommendations: This evaluation has demonstrated the degree to which Tebelopele's CT services vary from session to session. As counselors tend to focus on the initial questions on the intake sheet, it is important that TB screening questions be moved to the first section on the intake sheet, which is consistent with Tebelopele's TB policy. In addition, a check list of core components of the CT session should be mounted in each counseling room to guide and ensure completeness of the CT session.

PS-101470-15   Co-infection TB-HIV clinical management guidelines collaborate for the capture of data

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Background: Since 2003 the Dominican Republic started a joint plan for HIV-TB activities. The estimated general adult population HIV prevalence rate is 0.8% with more than 66 000 PLWHA. Recently in 2010 TB National Program Evaluation informs that in some provinces more than 20% of TB cases are HIV (+) more than last CENISMI study which is estimates that 8.6% of TB patients are HIV-seropositive. The health providers are not full training in clinical TB and HIV guidelines and a new register need to set up in the TB clinic setting for all patients diagnosed with HIV. The TB-HIV National Body Commission (CONACO) implemented the National TB-HIV Clinical Guideline focuses on collaborative activities at the local service delivery sites and at the community level in order to provide access to treatment and care for patients with HIV-TB co-infection.

Result/lesson drawn: A joint technical coordination body has been; national TB and HIV clinical co-infection guidelines has been discussed and validated, protocols for HIV-TB co-infection has been discussed and are being implemented at all level in the TB and HIV services in the health sector, Isoniazide and co-trimoxazole preventive therapy is part of the clinical service, and the document on the 'co-infection HIV/AIDS/TB clinical management guidelines' have been implemented. Computerization will take place at level national data collection and analysis to support health providers in TB-HIV co-infection throughout the country and to monitor and evaluate the implementation of these activities.

Conclusion: CONACO is an essential tool for coordination the interprogram activities to decrease the burden of HIV in TB patients; TB-HIV National Clinical Guidelines is part of training at all level health facilities. The experience accumulated in this process will improve the surveillance system and should be implemented throughout the entire country.

PS-101342-15   Experience of provider initiated testing and counselling for HIV in TB clinics in Zambia, 2007–2009

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Background: Zambia is faced with dual TB and HIV epidemics; 70% of patients undergoing TB treatment are HIV-infected. To optimize clinical outcomes and increase access to HIV testing, the Ministry of Health (MOH) prioritized provider initiated testing and counseling for HIV (PITC) in TB clinics in 2007. We present 3 year data and lessons learnt on program sustainability.

Methods: Trainings in PITC diagnostic algorithms and rapid HIV testing, using MOH guidelines, were rolled out for TB suspects in clinics in Lusaka. Communication and referral systems between TB and HIV clinics were strengthened to facilitate enrollment in HIV care for those testing positive. Post implementation data were collected from January 2007 until December 2009. A descriptive analysis of clinic records was performed.

Results: Over a period of 3 years 843 staff were trained in 22 district clinics and 21 206 TB suspects were counseled. Of those counseled, 12 749 (62%) were tested and 7608 (60%) were found to be HIV-positive. Patients with known HIV status did not undergo PITC. TB suspects counseled increased from 4974 in 2007 to 5145 in 2008, and 6455 in 2009; a 30% increase. Rates of testing acceptance over the same period were 83%, 69% and 79%. Patients with known HIV status prior to PITC increased from 6% in 2007 to 29% in 2009.

Conclusion: PITC in TB clinics is an effective and sustainable method to diagnose large numbers of HIV infected patients to be enrolled in HIV care and has high rates of acceptability in this population. Although there is an increase in patients with known HIV status there continues to be considerable need for ongoing HIV testing of TB suspects as shown by a substantial increase in PITC numbers. These results support the continuation of HIV testing in TB care centers.

CLINICAL TUBERCULOSIS: CASE MANAGEMENT/TREATMENT/ SURVEILLANCE

PS-100120-15   Does failure with fixed dose combination mean drug-resistant tuberculosis?

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Background: For the last many years, it was observed that significant numbers of tuberculosis patients treated with Fixed Dose Combination (FDCs) were not responding to treatment and were labeled as Drug Resistant Tuberculosis (DR-TB). It was hypothesized that treatment of these cases with separate drugs will improve the outcome.
Objective: To evaluate the response to separate drugs in patients who fail to respond to FDCs.
Methodology: Prospective study, from May 2006 to July 2008.
Setting: Ojha Institute of Chest Diseases, Aga Khan University Hospital & private practice. Included patients were suffering from tuberculosis (smear positive/ tubercular Pleural effusion & TB lymph node). They did not improve after receiving at least three months of four drug FDCs in adequate WHO recommended dose. The recruited patients were prescribed regimen consisting of Ethambutol and pyrazinamide as separate drugs and Rifampicin and INH as FDCs as per body weight. Clinical response was evaluated in all while microbiological & radiological parameters were evaluated where feasible.
Results: Out of total 94 patients 54 (57.4%) were male. The 56 (59.6%) cases were of Pulmonary tuberculosis, 16 (17%) TB Lymph node and 22 (23.4%) tubercular pleural effusion. All patients have used adequate four drug FDCs for adequate period and were compliant with the therapy. At the end of two months: Overall clinical response was adequate in 90 (95.7%) patients, among pulmonary cases, 40/56 (71.4%) converted smear negative, among pleural effusion cases, all improved clinically & radiologically and among TB lymph node group, node regressed in all 16 patients with healing of discharging sinuses of all six patients.
Conclusion: Patients who fail on FDCs should be given a trial of Separate Drugs anti-tuberculosis drugs before labeling DR-TB.

PS-100179-15   Intermittent TB treatment adherence is associated with poor long-term outcome

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Background: Default from tuberculosis (TB) treatment is associated with death, drug resistance and TB recurrence. Some patients do not default completely but rather take all of the prescribed TB chemotherapy in an intermittent manner, for poorly defined reasons and with unknown consequences. We studied the risk factors for intermittent adherence to TB therapy and then tested for associations with long term treatment outcome.
Methods: A cohort study recruited 411 pulmonary TB out-patients being treated in a government hospital in Lima, Peru from 1999 to 2003. Patients were treated with clinic-based DOTS by the national programme according to national and WHO guidelines. Intermittent adherence was defined as the 10% who took longest to complete the first 50 doses in their chemotherapy intensive phase. Risk factors and their odds ratios (OR) were identified using logistic regression. Patients were then followed up and interviewed after a mean of 5.7 years. Time-to-event analysis was used to test for effects of treatment intermittency on outcome.
Results: Patients took a mean of 58 days (52–118) to complete 50 treatment doses. In multiple logistic regression analysis, treatment intermittency was independently associated with HIV-TB co-infection (OR 8.8, $P = 0.02$), female sex (OR 2.5, $P = 0.04$), and young age (15–25 years OR 2.7, $P = 0.03$). At long-term follow-up, 14 (4.5%) of patients had suffered a recurrence of TB. Log-rank analysis demonstrated that intermittent treatment adherence was associated with TB recurrence in univariate analysis ($P = 0.04$, see
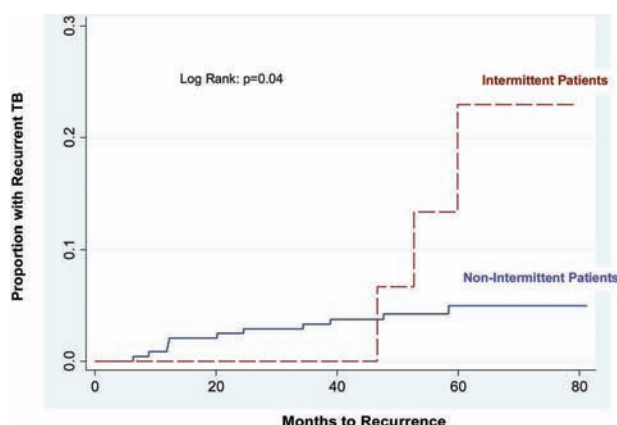

Figure Intermittent adherence is associated with TB recurrence.

Kaplan-Meier graph) and in Cox proportional hazards multivariate analysis (Hazard Ratio 4.0, $P = 0.04$).

Conclusion: Patients with HIV co-infection, women and younger adults are significantly more likely to exhibit intermittent treatment adherence during the intensive phase. Furthermore, patients who complete therapy but with intermittent adherence during the intensive phase are at an increased risk of subsequent TB recurrence.

PS-100292-15   Evolution du gain de poids des tuberculeux sous traitement et pronostic

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L'OMS encourage l'implication de la communauté dans la prise en charge des tuberculeux. Mais, les agents communautaires n'ont pas reçu de formation initiale sur la tuberculose. Alors, ils devraient disposer de moyens simples et efficaces pour assurer le suivi clinique des tuberculeux à leur charge. Cette étude vise à déterminer l'intérêt et la validité de la

Figure Evolution du gain de poids des tuberculeux selon l'issue médicale.

courbe de gain de poids (GP) sur le pronostic des tuberculeux en cours de traitement. Une étude sur un petit échantillon allant dans ce sens a été déjà effectuée. Une analyse longitudinale du gain de poids des malades durant le traitement a été menée. Cette étude a ciblé les malades pris en charge par 3 centres de diagnostic et de traitement de la tuberculose sur une période de 5 ans (1er Janvier 2003 au 31 Décembre 2007). Au total, 3887 dossiers ont pu être exploités dont 3597 ont réussi le traitement, 68 cas d'échec et 222 cas de décès au début de l'étude. La différence entre le GP moyen des cas de réussite et celui des cas de décès est significative dès le premier mois ($P < 0,05$), quelle que soit la forme clinique (Box 1). Le GP des cas de réussite présente une évolution ascendante. Au premier mois, ils ont gagné en moyenne 1,5 kg, au deuxième mois 2,6 kg, au cinquième mois 4 kg et au septième mois 4,6 kg. Alors les cas de décès, au lieu de gagner de poids, ils en perdent et présentent une courbe décroissante dès le début du traitement. Le GP des malades ayant échoué le traitement suit celui des cas de réussite jusqu'au 2ème mois. Il stagne et devient décroissante à partir du 5ème mois.

Cette étude confirme que la courbe du gain de poids constitue un outil fiable pour le suivi des tuberculeux. Elle va être facile à utiliser par les agents communautaires. Un patient ne gagnant pas de poids doit être référé au centre spécialisé en vue d'une prise en charge spécifique. Cette approche va contribuer à la réduction de la létalité et éventuellement à la réduction de l'échec du traitement.
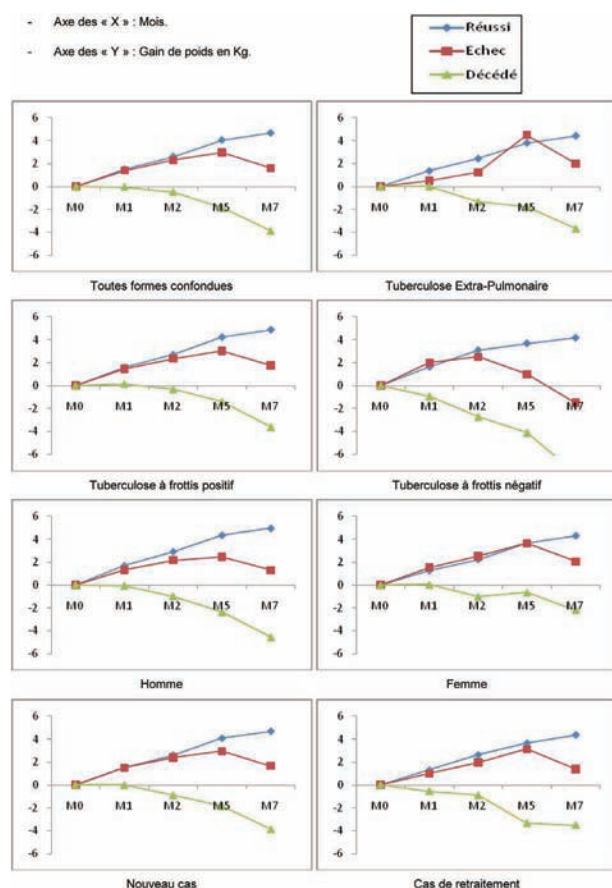
PS-100505-15   Design for housing and treatment of refugees with infectious tuberculosis in Nepal

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Background: Beginning in 2007, International Organization for Migration (IOM) conducted medical screening of approximately 30 000 Bhutanese refugees from seven camps in southeastern Nepal. Of these, the prevalence of culture-confirmed pulmonary TB was 664 per 100 000. Resistance to at least one TB drug was identified in 13% of cases. Risk of TB transmission in this setting was high due to overcrowding and poor ventilation in the refugee shelters.

Methods: To reduce risk of TB transmission in this low-resource setting, a housing and treatment center was designed with natural ventilation. Indications for admission were defined as TB patients with sputum smear yielding acid fast bacilli (AFB) of 2+ or greater, sputum culture yielding MDR-TB, children <5 years old in the household, or inability to attend daily observed therapy (DOT) clinics in the camps. Indications for discharge were defined as negative AFB

smear for those with pan-susceptible TB, and negative culture for those with MDR-TB. Patients were to receive daily DOT, regular counseling and routine physician visits.

Results: A housing facility was built with nine individual huts of locally available materials, each with an area of 15.9 m² and three windows. With prevailing winds of 4.6 km/hr, measured natural ventilation was 58 ACH. A total of 19 patients have lived in the TB housing center, including three patients with MDR-TB. Of these, 13 (68%) were discharged and two (11%) died. Follow-up cultures from patients who had converted to negative were all negative, indicating no transmission of TB between patients.

Conclusion: Inpatient housing for treatment of TB in a refugee setting was built with predominantly natural ventilation to reduce risk of TB transmission. Evidence from initial 3-year period suggests that the facility achieved goal of isolating infectious TB patients from community, providing DOT in setting amenable to patient compliance, and not resulting in nosocomial transmission.

PS-100517-15   The emotional representation of tuberculosis related to treatment seeking and medication adherence

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Aim: Tuberculosis morbidity and mortality are worsened when people delay seeking treatment or do not take their medications as prescribed. No known studies have explored the relationships between emotional representation (the emotions a person associates with TB) and illness coherence (how well a person understands their TB) with illness representation (a person's mental image of their TB), stigma, delay in seeking treatment, and medication adherence in Russians with pulmonary tuberculosis.

Methods: We used a descriptive correlational design to perform a secondary analysis of an existing dataset. In the original study, a self-administered survey was given to 105 adults, ages 18 and older, who were diagnosed with and being treated for active pulmonary tuberculosis at two outpatient TB clinics in Russia.

Results: Strong negative emotions were correlated with the perception that TB carried serious consequences (r = 0.543, P = 0.001) and with all stigma subscales: social rejection (r = 0.625, P < 0.001), financial security (r = 0.473, P < 0.001), internalized shame (r = 0.350, P < 0.001), and social isolation (r = 0.648, P < 0.001). People who believed they understood their TB were less likely to experience strong negative emotions (r = −0.264, P = 0.007). Social isolation and consequences were predictors of strong negative emotions (F (4,89) = 21.27, P < 0.01.) and accounted for 47% of the variance in

emotions. Emotions and understanding of TB were not associated with treatment delay or adherence to medications.

Conclusions: As patients feel more informed about their disease and treatment program, negative emotional and social consequences of the disease tend to decrease. It is the role of health care professionals to ensure that patients receive adequate education and psychological support; this role requires preparation. Development of programs preparing health care workers to identify and treat emotional responses associated with tuberculosis is recommended.

PS-100660-15   Oral desensitization to intravenous PAS in a case of PAS allergy in MDR-TB

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Introduction: Paraaminosalicylic acid (PAS) is commonly used in multidrug-resistant tuberculosis. Since its first use in the 1950s, hypersensitivity reactions frequently limited its use in clinical practice. Cases of successful desensitization against PAS using orally administered paser granules in ascending doses are described in the literature (Int J Tuberc Lung Dis 2003; 7: 493). These granules, however, are not readily available in Germany.

Case report: A 25 years old patient with severe multidrug-resistant smear positive bilateral lung tuberculosis (in vitro resistance against all first line drugs) developed drug fever with rash, acral cyanosis and shivering 3 times after intravenous application of 13.49 g PAS. Hard gelatine capsules with PAS dry substance intended for intravenous use were produced in order to desensitize this patient. Encapsulated PAS was applied in rising doses starting with 10 mg per day and doubling the dose every 2 days until the half maximal dose of 5120 mg was reached. Then we switched to intravenous application of full dose PAS (13.49 g/day) and the treatment was well tolerated. In a 32 weeks follow-up no more allergic reactions were encountered.

Conclusions: PAS dry substance encapsulated in hard gelatine capsules and administered orally in rising concentrations may be used to successfully desensitize against intravenous PAS. Within 21 days full doses of intravenous PAS were tolerated without a need for corticosteroids or corticotropins.

PS-100855-15   Determinantes sociales de la no-adherencia al tratamiento de la tuberculosis en Argentina

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Antecedentes: En la Argentina, cada año se diagnostican más de 10 000 nuevos casos y mueren más de 800 personas a causa de la TB. La administración del tratamiento completo constituye una de las principales herramientas para el control de la enfermedad. La evidencia indica que además de la modalidad de tratamiento, las características socio-demográficas de los pacientes inciden en el éxito o fracaso del tratamiento.

Diseño y metodología: Estudio de caso-control realizado en el AMBA sobre pacientes diagnosticados en 2007, residentes y atendidos en hospitales de municipios seleccionados. Los casos ($n = 38$) fueron los pacientes no-adherentes y los controles ($n = 85$) fueron los pacientes adherentes. La información sobre adherencia se recogió de los registros del Programa Nacional de Control de la TB. Los datos sociodemográficos se recolectaron mediante un cuestionario específicamente diseñado. El análisis de los factores predictivos de la no-adherencia se llevó a cabo mediante la regresión logística.

Resultados: El 98,4% de los pacientes realizaron tratamiento autoadministrado. Los pacientes cuyas viviendas no contaban con agua, tuvieron casi 3 veces más probabilidad de no-adherencia que los que vivían en viviendas que sí contaban con agua (OR: 2,8; IC95% 1,1–6,9). Los pacientes que realizaban los controles en un hospital tuvieron 3 veces más riesgo de no adherir al tratamiento que aquellos que los realizaban en los centros de atención primaria de salud (OR: 3,2; IC95% 1,1–8,9).

Conclusiones y recomendaciones: La pobreza extrema reduce la capacidad de adherir al tratamiento. Es necesario evaluar qué características de los servicios de salud reducen la posibilidad de completar el tratamiento.

PS-101194-15   Decentralisation of TB-HIV services in Swaziland: best practices

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Aim: To document best practices in decentralized TB-HIV services to the rural.
Background: Poor access to TB-HIV services due to centralized system is a major problem in Swaziland where the HIV/AIDS and Tuberculosis epidemics are threatening the Swazi people. TB incidence rate 1198/100 000 population, and TB-HIV co-infection rate amongst TB patients is 80%. This is further complicated by increasing number of MDR-TB cases.
Method: Decentralization, patient centered model adopted, to ensure accessibility of TB-HIV services to people at grass root level in the Shiselweni region. We identified six peripheral clinics in the region with a high patient load to provide TB-HIV services. These clinics were accredited to basic management units. TB treatment initiation and ART refill was task shifted to nurses. Expert clients and community treatment supporters performed TB screening, patient education and defaulter tracing. HIV counseling and testing was conducted by lay counsellors. Motor bikes were used to transport sputum and blood samples from clinics to the laboratory. Measurement of accessibility based on increased case detection and proportion of TB patients tested for HIV.
Results: The case detection rate for new smear positive cases increased significantly from 65% in 2008 to 86% in 2009. HTC uptake amongst TB suspects and patients improved from 64% in 2008 to 76% in 2009.
Conclusion: Implementation of decentralization and task shifting within the health care system has improved accessibility to TB-HIV services and can be replicated to all regions in the country.

PS-101221-15   Outcomes of a systematic approach to managing loss to follow-up in London

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Background: Loss-to-follow up (LFU) prior to tuberculosis (TB) treatment completion is a major challenge to TB control internationally, especially among hard-to-reach patients with complex social problems. Despite this, no internationally agreed standardised definition or clinical management guidance for LFU exists. We have developed a working definition and a systematic approach to managing LFU and returning patients to treatment services.
Method: We reviewed all TB patients referred to Find&Treat, a pan-London specialist TB outreach service, who were LFU at any point in treatment. Information on treatment delivery (directly or self observed), risk factors, smear status, drug susceptibility and treatment interruptions, clinical management and outcomes were collected.
Results: In total, 169 active TB LFU patients were reviewed. 122 (72%) had pulmonary TB, of which 64 (53%) were sputum smear-positive. 25 (15%) had drug resistant disease of which 17 were sputum smear positive. 73% of LFU cases had a history of

homelessness, 60% had drug and alcohol issues and 48% had a history of imprisonment. Cases were classified as either treatment completed, treatment stopped, transferred out, treatment re-established, treatment still chaotic, dead or still LFU. In total 123 (73%) of cases were successfully located.

Conclusions: Returning LFU TB patients to treatment services is an essential component of metropolitan TB control. Our approach demonstrates that in most cases it is possible to find and return hard-to-reach patients to clinical services. This work highlights the potential public health impact of LFU infectious and drug resistant cases and variations in clinical practice following unplanned treatment interruptions.

PS-101252-15 The epidemiological context after 9 years of DOT in the 4th sector of Bucharest

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Background: The 4th Sector of Bucharest has 300 000 inhabitants, representing almost 16% of the entire town's population.

Objective: We made a retrospective study of the evolution of the main TB endemic indicators at 9 years after applying DOT in the 4th Sector.

Material and method: Use of data existing in the TB Register, electronic TB register and in other official records of the information system regarding the epidemiological surveillance.

Results: A decrease of 30.9% in the number of the newly recorded patients (307–2000 and 212–2009) occurred between 2000 (year of DOTS implementation) and 2009. 30% of the pulmonary TB patients registered were unemployed. A percent of 66.8% of the new patients recorded in 2009 with pulmonary tuberculosis were confirmed bacteriological. TB cases among the infant population diminished from 46/1000 (2000) to 16.9/1000 (2009). The therapeutically success rate of the source cases (pulmonary TB with M+), 2008 cohort, was situated at 86.3%. The TB mortality decreased from 4/1000 in 2008 to 2/1000 in 2009, the last explained by the existence of some extended forms at detection, associated diseases and a social status of homeless. Prevalence of primary MDR was 3.3% in 2009.

Conclusions: Although the evolution of the main indicators of the TB endemic in the 4th Sector of Bucharest is favorable mainly due to the DOT implementation, the involve of some vulnerable category (old people, unemployed, homeless, etc.) remaines a priority among the measures of TB control in the territory. The increase of the rigor in applying all the TB control measures will contribute to improve the endemic continuously.

PS-101333-15 Results of bronchial artery embolization for life-threatening haemoptysis in active pulmonary TB

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Objective: To determine immediate and long term results of BAE in patients with active pulmonary tuberculosis.

Design: A retrospective analysis.

Setting: Metro Centre for Respiratory Diseases.

Patients: Fifteen sputum positive pulmonary tuberculosis patient's with life threatening hemoptysis admitted between January 2004 to December 2007 analysed.

Method and measurements: The mean age of patient was 42.8 year (14–71 years) with follow up period between 24 –74 months (median 52 months). All had smear positive pulmonary tuberculosis at admission with massive hemoptysis. The associated diseases included Aspergilloma = 4, Unilateral Bronchiectasis = 4, Bilateral Bronchiectasis = 3. Twelve patients had taken ATT in past. Three had MDR tuberculosis. All patients underwent CT thorax and bronchoscopy and after localizing bleeding site underwent BAE within 48 hrs of admission. Immediate control of bleeding was achieved in 14/15 patients (93.4%). 13/15 patients (86.7%) continued to be asymptomatic without recurrence till 24 months (minimum follow up).

Conclusion: BAE is effective in immediate and long term control of massive haemoptysis in patients with active pulmonary tuberculosis.

PS-101415-15 Integration of nutrition indicators into routine TB surveillance: challenges and opportunities

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Background: Tuberculosis poverty and malnutrition are closely associated. 56% of Kenyans are estimates to live below the poverty line while 13% are malnourished with significant variations in different TB control Regions. In 2009 the national TB program in recognition of the role nutrition plays in Treatment completion and adherence initiated integration of Nutritional indicators into the routine recording and reporting.

Methods: We abstracted nutritional indicators from the national database and interviewed 24 district coordinators 2 from each of the 12 TB control regions on the use and understanding of the nutritional indicators.

Results: From the notification data not all regions reported on the nutrition indicators reported. The

numbers of patients receiving nutrition support were higher than number of malnutrition cases identified. 1.08% (1115) of the total 110 015 TB patients reported were severe to moderately malnourished where only 3.90% of the total received support. Only 50% (12) of the interviewed DTLC's had clear understanding of the nutritional indicators, with 35% (8) having clear understanding of the relationship between TB and nutrition.

Conclusion: Integration of nutrition into the routine TB programming is a new concept in Kenya which requires clear implementation plans since after the roll out of the Nutrition in TB strategic guidelines and incorporation of the indicators it is clear that there is malnutrition amongst TB patients although the true burden is not yet known, knowledge gap in nutrition which needs to be addressed urgently and equipments to undertake nutritional assessment need to be procured for all treatment sites.

### PS-101476-15 Household natural ventilation influences the risk of tuberculosis transmission

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Background: Ventilation is a key determinant of the risk of airborne TB transmission putting patients' household contacts at high risk of TB. We therefore studied the association between household ventilation and secondary TB incidence in a Peruvian shantytown.

Methods: For a case control study, homes were selected in which a primary case of sputum smear microscopy positive TB had ($n = 26$) and had not ($n = 30$) led to subsequently confirmed TB disease in at least one contact residing in the same house. Of these, 20 homes were excluded because structural modifications had been made in the median 3.5 years since the index patient TB diagnosis. Using a CO2 gas tracer technique the absolute ventilation (AV) of each home was measured under two conditions: (1) 'typical', as the doors and windows were normally maintained at the time of diagnosis, and (2) 'open', with all doors and windows completely open.

Results: The AV was found to be significantly lower in homes with secondary TB than in homes without (median 1300 m³/hr vs. 2400 m³/hr respectively, $P = 0.02$). Homes without secondary TB had a wide range in AV (200–4500 m³/hr) whereas there were no homes with secondary TB and typical AV greater than 2050 m³/hr. Completely opening windows and doors in homes in which secondary TB occurred changed AV from median 1300 to 3200 m³/hr ($P = 0.007$),

increasing ventilation to a level similar to the homes in which secondary TB had not occurred. For a typical outbreak patient as defined by previous research, the TB transmission risk estimated by the Wells-Riley equation was 7.5%/day in homes in which secondary TB did not occur compared with 13%/day in homes with secondary TB ($P = 0.04$), which fell to 5.6%/day when homes had all windows and doors open ($P = 0.008$).
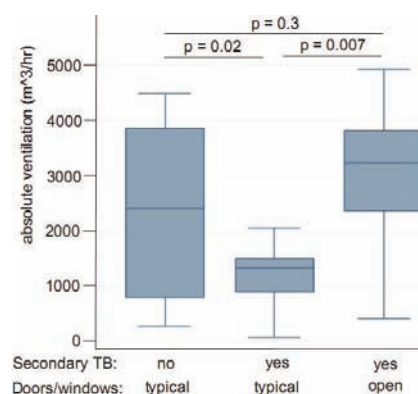
Conclusion: TB disease among household contacts was more likely in poorly ventilated homes. Opening windows and doors halved estimated transmission risk and thus may reduce TB disease transmission in TB affected house.

PS-100348-15 TB in a university hospital of Italy over ten years: clinical features and treatment outcomes

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Setting: Treatment outcome is a critical problem in TB management, so that WHO in 1993 recommended that the impact of TB control programs should be monitored and suggested to introduce surveillance in the treatment outcomes. In Italy, very few data about treatment outcomes are available, except prospective data from the WHO-AIPO initiative.

Aim: To describe the clinical features and treatment outcomes of all patients discharged from the Infectious Diseases Unit of the University Hospital of Pisa over a ten year period (1999–2008).

Design: A total of 220 patients diagnosed with TB were examined, 126 of them were males, 121 immigrants; median age was 50 years, a big part were far from Pisa area (104/220).

Results: In 94 cases there were at least one extrapulmonary localization, 82 were smear positive; 24 cases were HIV positive, in 6 of them a MDR strain was found. Eighty-four of them (38%) were lost to follow up one month after discharge (early lost). There was a significant association between early lost and the

area of residence of the patient (51/ 84 patients, 61%, lived outside the greater Pisa area, $P < 0.05$). Nine patients (4%) died (7 of them during hospital stay). There was a significant association between risk of death, italian nationality and age; using multivariate analysis, only age entered the model. A successful treatment outcome leading to withdrawal of treatment (according to the clinical evaluation) was reported in 42% (73% in patients that continued the follow-up after the first month). No association was found between successful outcomes and clinical findings at diagnosis.

Conclusion: The rate of lost is high in this population and the rate of successful outcome is far from the WHO target of 85%. There is need to implement communication between clinicians, laboratory, public and preventive health services in order to strengthen surveillance systems, to evaluate the impact of the surveillance policy and to improve TB control.

PS-100161-15   Surveillance of MDR-TB, experiences using courier services in Central Province, Kenya

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Background: The WHO estimates that in Kenya, 7.9% of all retreatment cases and 1.9% of all new cases of TB are MDR-TB. The last DRS in Kenya did not find any MDR-TB cases but this has now changed as Kenya now has MDR-TB cases. Access to sputum culture and DST is limited as only one central laboratory can do this. This abstract shows that this barrier can be cut using courier system and effective surveillance.
Methods: A local courier service firm was contracted to transport sputum specimens from the peripheral health facilities to the central reference laboratory. All patients under retreatment across all health facilities have their sputum samples taken, sealed and labeled and taken to the courier office same day. For the centers without any courier service, the sample is transported by a staff to the nearest courier service office. The courier delivers the samples to the central reference laboratory in less than 24 hours.

Results: This surveillance began in late 2007, the province had 581 retreatment cases for which 104 (18%) were taken with no case of MDR-TB. In 2008, 601 (80%) out of the 749 retreatment cases and 690 (88%) of the 783 retreatment cases in 2009 had sputum send for culture and DST. In total, 6 MDR-TB cases (5 are HIV negative and 1 HIV positive) have been diagnosed in 2008 and 2009.
Conclusions: It is possible to effectively do surveillance for MDR-TB using courier services in Kenya hence cutting the barrier of accessing these services. However, we need to expand surveillance to all new TB cases to effectively detect most of the MDR-TB cases.

PUBLIC HEALTH/SPECIAL POPULATIONS

PS-101401-15   Morbidity and mortality surveillance in preparation for future TB vaccine trials in Western Kenya

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Background: Phase III TB vaccine trials require solid measurable endpoints and large sample sizes. Scheduled active follow up visits may not be timely enough to capture all TB cases, suspects and deaths. Vital registration in high burden TB countries are often insufficient. Surveillance systems may be needed to supplement scheduled follow up visits.
Setting: An adolescent TB incidence cohort in Karemo division, western Kenya. The study area is part of a Health and Demographic Surveillance System (HDSS) which records the population's demographic characteristics and vital events, including births, deaths and migration.
Objective: To assess whether health and vital event record surveillance will detect additional TB suspects, cases and deaths that are missed or not yet captured by the 4-monthly scheduled follow-up visits.
Methods: TB registers at the health facilities within the study area are searched weekly. TB cases residing within the HDSS are matched with their HDSS residence to see if any study participants share the same households as the registered TB cases. The participants are then contacted for verification and investigation as TB suspects. HDSS vital event registers are consulted fortnightly, mortuary records and chief's records are searched bi-annually for participants who are lost to follow up.
Results: Since June 2009, the morbidity surveillance system has identified 96 TB suspects: 2 from chest X-ray records, 3 from TB laboratory records and 91 through TB treatment registers. All these suspects and

one TB case had not been picked up during scheduled follow-up visits. The mortality surveillance so far identified 5 deaths among study participants, which were reported by HDSS workers, and 3 verbal autopsy reports have been obtained from the HDSS.

Conclusion: The surveillance activities identified a large number of TB suspects through health records searches. The usefulness of this tool for TB vaccine trials should continue to be explored.

PS-101402-15   Modelling of smear-positive tuberculosis treatment outcomes of cases notified in Kenya, 2002–2007

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Background: The number of TB cases notified in Kenya has increased tenfold since 1990 while the TB incidence of infectious forms TB increased from 32 per 100 000 in 1990 to 108 per 100 000 in the year 2007. Despite significant progress in TB control, the emergence of MDR-TB calls for understanding the dynamics of treatment outcomes of the infectious forms of tuberculosis over time in the country.

Methods: We abstracted the national notification data for the years 2002–2007. This was modelled using poisson and multinomial logistic regression looking at the rates and odds of occurrence of the treatment outcomes across the provinces over the years.

Results: Modelling showed that rates of occurrence of the treatment outcome cure were 1.415 times higher in the year 2007 as compared to the year 2002 as shown in table1&2. Deaths were 0.919 times lower in 2007 relative to the year 2000. Multinomial modelling for failures relative to deaths the odds of failures relative to death was lower across all provinces except North Eastern province where the odds of failures relative to deaths was 1.59 times higher than Nairobi.

Conclusions and recommendations: The results demonstrate improved treatment outcomes over the years which corroborate efforts that have been put in place such as policy changes to combat the rising cases of tuberculosis. The upward trend of treatment failures highlights the risk of MDR-TB cases. There is need to sustain the national response to TB control. The threat of MDR-TB calls for requisite policies and resources.

PS-101435-15   Epidemiology of non tuberculous mycobacteria infection in upper north of Thailand

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Background: Non-tuberculous mycobacterial (NTM) infection is an important cause of opportunistic infection in HIV/AIDS patients. Thailand has high infection rate of HIV but there was no any study to determine the problem of NTM infection.

Objective: To study epidemiology of NTM infection in upper north of Thailand.

Method: Cross sectional study was conducted in tuberculosis suspected patients who came to public hospitals in 8 upper northern provinces. All cases who had sputum smear positive from April 2008 to September 2009 were included in the study. Sputum sample from each patient were sent to Central Laboratory, Office of Disease Prevention and Control 10th for culture and identification. Identification was done by molecular technique.

Result: From 3325 cultures which positive for mycobacteria during study period, 253 (7.6%) cultures were NTM. Mean age was 45 year old, male:female was 2:1 and infected with HIV 14.1%. High NTM infection rate was found in Chiangrai, Lampang and Nan province as in Table.

	Province								
	CM	LP	LPa	PY	CR	MS	PR	Nan	Total
% of NTM	5.3	8.4	9.8	6.9	10.5	6.8	7.6	9.0	7.6

Conclusion: High NTM infection rate of 7.6% in new smear positive tuberculosis patients in this region will have a great impact on treatment success outcome because most of NTM resist to all anti-tuberculous drugs. The estimated loss of 10 million Baht for drug cost, income deficit and opportunity loss were calculated in this situation instead of invest 2 million for identification and improving outcome of treatment.

PS-101493-15   Frequency and timing of tuberculosis recurrence in Western Cape Province, South Africa

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Setting: Two urban communities in Cape Town, Western Cape Province, South Africa with annual tuberculosis (TB) notification rates exceeding 1000 per 100 000 (all cases). Rates of TB re-infection were shown to be high in these communities.

Objective: To estimate the risk of recurrent treatment for different groups of TB cases; to analyse the distribution of time to re-treatment.

Methods: We analysed 1996–2008 routine TB register data from 2 TB clinics. Probabilistic linkage software was used to identify individual subsequent treatment episodes. Matches identified were manually reviewed by 2 independent data managers. We estimated 5-year risks of recurrent treatment for the 1996–2003 cohort of bacteriologically confirmed cases. For 621 cases with available data, time intervals between treatment end date and record date of a subsequent episode were analysed.

Results: A total of 3118 confirmed TB cases were recorded. The estimated 5-year risk of recurrence was 20.1% (95%CI: 18.1%–22.1%) for all TB cases, 15.3% (13.2%–17.4%) after cure, 40.0% (22.9%–57.1%) for HIV-positive cases after cure, and 37.6% (31.4%–37.9%) after default. We found a Gaussian distribution of treatment intervals with a peak at 5.0 months (standard SD: 1.6 months), and, underlying this distribution, a slow exponential decay with the number of cases decreasing at 3.2% per year. Strong evidence was found for a difference in the fit of the 2 distributions compared to a single exponential distribution ($P < 0.001$). Treatment default accounted for 76 (32.9%) of 231 cases with a subsequent episode recorded within 8 months since treatment end date.

Conclusions: TB recurrence seems highest among treatment defaulters and HIV co-infected individuals in this setting. A high number of cases with recurrent TB present early after the end of previous treatment. We speculate that follow-up examinations within the first 6–8 months after the end of treatment may be a useful strategy to early identify recurrent TB.

PS-101495-15   Poverty and poor nutrition are the strongest risk factors for TB disease following exposure

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Background: People living with TB patients are at high risk of developing TB disease in the first years after exposure. We aimed to characterize predictors of this risk in a Peruvian shantytown.

Methods: Newly diagnosed patients ($n = 708$) with sputum that was smear microscopy positive for TB were identified. Their contacts aged over 14 years were recruited and followed in a prospective cohort study for up to 5 years. Risk factors were determined at the time of recruitment and a socioeconomic score was made using tetrachoric factorial analysis of data including assets and basic services. The association of these variables with subsequent TB disease was assessed using Cox regression analysis clustered by household. This determined hazard ratios (HR) for secondary TB risk with 95% confidence intervals (CI).

Results: Among 1984 household contacts, we confirmed 110 secondary TB cases. Secondary TB risk is shown in the graph and was higher among the poorest households. Specifically, people living in the poorest third of households had 1.7 times the HR of secondary TB compared to the least poor third of households (CI 1.1–2.9, $P = 0.05$). This association was mediated by crowding but the number of people sharing each room was not independently associated with TB risk. Underweight predicted secondary TB (BMI < 20 kg/m² HR 1.7, CI 1.1–2.7, $P = 0.03$) compared to normal BMI, and overweight was protective (BMI > 25 kg/m² HR 0.40, CI 0.24–0.63, $P < 0.001$). Contacts who had had previous TB were at
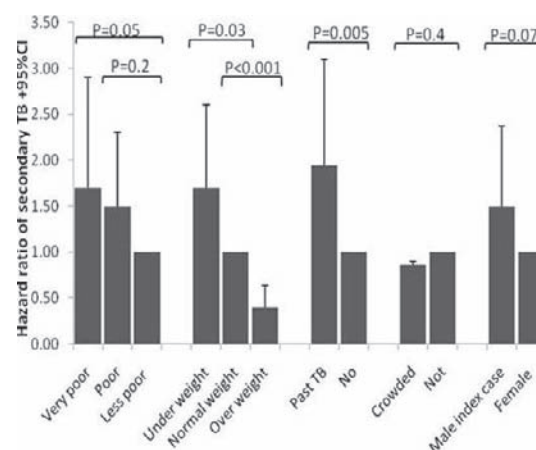
increased risk of secondary TB (HR 1.9, CI 1.2–3.1, $P = 0.005$), as were contacts of male index cases (HR 1.5, CI 0.95–2.2, $P = 0.07$). TB in household contacts was not significantly associated with BCG vaccination, the sex and age of the contact, or microbiological studies.

Conclusion: Poverty, under-nutrition and previous TB were the strongest risk factors for household contacts developing TB disease. These risk factors may be used to focus screening and preventive therapy.

PS-100632-15   Case detection under the national tuberculosis prevalence survey in Bangladesh

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Aim: Bangladesh has completed a national prevalence survey of smear positive cases among ⩾15 years population in 2009. The activities included active screening for TB cases through household survey. Experiences in conducting active screening for TB cases are described.

Methods: The survey included over 52 000 adults from about 22 000 households. Equal numbers of urban and rural clusters were selected. All members ⩾15 years were approached and two sputum samples were collected. Cases were diagnosed by Initial fluorescence microscopy, and then confirmed by Ziehl-Neelsen method.

Results: Census included 63 715 adults, 51% and 49% from rural and urban clusters respectively and almost equally from female and male. 81% provided at least one sputum sample and 5% had a history of cough. Among 11 617 non participants, 60% were male, around 70% were <45 years and 2.3% had a history cough. Thirty-three TB cases were detected, 15 of them complained of cough, and 3 were under TB treatment. In the collected sample 40% were actually sputum, even though macroscopically labeled as saliva. Absence of male members, difficulties in collecting samples from females, problems in entering urban apartments, resistance by religious leaders were some of the challenges faced. Programmatically, rapid deployment in a cluster, accommodation for short period, little time to build rapport, setting field laboratory in absence of regular water and electricity supply and keeping the staff healthy in a roaming field situation were major challenges.

Conclusions: A good team build up and intense communication between supervisors helped in conducting the survey smoothly. Continued and sustained backup from NTP and partners was useful to overcome these challenges.

PS-100399-15   Aspects épidémiologiques des cavernes tuberculeuses au CHU de Befelatanana

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Contexte : La tuberculose représente un grave problème de santé publique à Madagascar. Elle augmente dramatiquement dans le monde et est responsable de 1,7 millions de décès enregistrés en 2006. Les cas hospitaliers sont souvent de diagnostic tardif.

Objectifs : Déterminer les aspects épidémiologiques des cavernes tuberculeuses observées dans l'unité de soins, de formation et de recherche en pneumologie, au Centre Hospitalo-universitaire de Befelatanana durant la période de janvier 2006 à Décembre 2007.

Méthodologie : Il s'agit d'une étude descriptive rétrospective à partir des dossiers médicaux des malades pris en charge dans le service sur une période de deux ans.

Les paramètres à analyser sont : La prévalence , l'âge, le sexe, le niveau d'instruction, les facteurs de risques associés, la densité bacillaire, les caractéristiques radiologiques (taille, siège), le délai de dépistage. Les données ont été encodées sur Epi-info.

Résultats : Sur 214 malades recensés, 96 ont présenté des cavernes soit 44,85%. Le sexe ratio est de 1,2.

- L'âge moyen est de 40 ans [115–55 ans].
- 82,3% des malades avaient plus de dix BAAR par champ à l'examen microscopique.
- Les lésions se situaient le plus souvent au niveau du sommet droit (59,4%), unilatérales (92,7%), atteignaient généralement un lobe (94,8%).
- La plupart des cavernes ont une taille inférieure à cinq centimètres de grand axe (79,2%)
- L'intoxication tabagique est retrouvée dans 40,6% des cas.

Conclusion : La caverne tuberculeuse touche surtout les sujets jeunes de 25 à 40 ans. Pour avoir un dépistage précoce, nous recommandons une radiographie systématique du thorax au cours des visites médicales scolaires ou lors des visites d'embauche. Par ailleurs la lutte contre le tabagisme s'impose car il constitue le facteur de risque le plus fréquent.

PS-100608-15   No more re-emergence of tuberculosis in Cuba: lessons learned

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Background: Notification of pulmonary tuberculosis smear-positive pulmonary [TBpAFB (+)] cases as well as smear-negative declined to 6.4 per 105 population in 2006, really being a challenge for the Cuban society which is now facing its possible elimination.

Objectives: To describe and analyze former and re-

cent changes in some epidemiologic indicators and its influence about health policies and strategies on TB control.

Methods: Data of TB surveillance system in Cuba were collected and analyzed coming from the National Board of Statistic of the Ministry of Public Health. Absolute and relative numbers on TB and TB-HIV incidence in 1991–1994 and 2004–2008 were analyzed.

Results: The Cuban gross domestic product declined from 30 507.1 millions USD in 1990 to 21 160.3 millions in 1995 do to changes in the East European countries and economic blockage, whereas the reported Incidence Rate (IR) of TBp new cases increased from 4.7 to 14.7 per 105 respectively in 1991–1994. The inclusion of [TbpAFB (−)] cases in the compulsory report brought 24% increase of TB cases notification in 1994. In 2004–2008 speed of the annual mean reduction of IR stopped but rather a slight increase occurred. In children IR raised up from 0.3 to 0.5 per 105. The TB-HIV/Aids raised from 3.1% to 4.9%.

Conclusions: After the decline of TB in 1996–2006, the annual mean reduction of TB IR has stopped and then lessons were learned. Both, health and government authorities, have being enough alerted themselves as to plan new re-interventions to prevent possible reversion of TB epidemiological situation and to keep on going through elimination stages.

PS-101178-15   Estimation of tuberculosis burden in resource-limited settings: a capture recapture study from Yemen

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Background: Capture-recapture analysis has been used to assess the completeness of notification of various infectious diseases, including tuberculosis. This study aimed at determining the extent of TB case ascertainment by national TB programmes (NTP) and non-NTP providers through record linkage and estimating TB incidence using capture recapture analysis.

Design/methods: A prospective study was conducted in 12 randomly selected governorates whereby modified suspect and laboratory registers were introduced in all public and private non-NTP health facilities delivering care to TB patients during the period 1 February–30 April, 2010. Following mapping of all non-NTP facilities in these governorates, district coordinators distributed the registers and performed regular supervisory visits to ensure data quality and collect the forms. Record linkage was then conducted between these newly developed data sources and the existing electronic NTP data register to determine the proportion of case ascertainment and estimate the total number of TB cases using capture recapture technique.

Results: During the pilot phase conducted in 4 governorates in 2008, a total of 113 cases were diagnosed by non-NTP providers compared to 378 during the same quarter. The proportion of cases detected by NTP accounted for 92.1% of cases detected in the health system. The case detection rate using the 2 data source capture recapture reported a case detection rate of 67% for sputum smear positive TB.

Conclusion and recommendations: Inventory and capture recapture studies provide useful methods for estimating TB burden in low and intermediate burden countries. To address two way dependency between data sources, a 3 source capture recapture technique using loglinear modelling will be applied on the expanded study conducted during 2010.

PS-101537-15   Analysis of tuberculosis situation in Nepal, 1996–2009

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Rationale: About 45% of population is infected with TB, 40 000 TB cases occur annually among these 20 000 are infectious and 5000–7000 deaths are attributed to TB. The surveillance system of TB at national level shows variation from year to year. Over time the gap of notified incidence and expected incidence of TB is reducing.

Objective: To explain the disease estimate of TB in Nepal by using regular surveillance data.

Methods: An analytical study of TB surveillance data for 1996–2009 periods was done using least square meathed. Linear regression is calculated and paired t-test used for comparison of notification and expected TB incidence of all forms of TB using SPSS package.

Results: During the study period reported TB incidence of all forms was 136/100 000/year in 1996 while 125/100 000/year in 2009. Overall decreasing trend of TB incidence is 0.812/100 000 annual by an equation IRt = 113.925–0.812*t ($P < 0.001$). The model will remain valid if HIV situation remains stable in the country. Reported incidence in comparison with expected incidence during this periods shows that TB is still a public health problem in Nepal (t-test < 0.001). Reported incidence of male TB patients is almost double and incidence rate is different among age groups i.e. still higher in young age groups how-

ever steadily shifting to older age groups. The notified incidence and expected TB incidence is also significantly decreasing during study period.

Conclusion: Reporting incidence is decreasing annually however study finds that TB is still a public health problem in Nepal. The equation can also provide future information to guide program planning and management in order to achieve programme goals and targets.

PS-101533-15   Áreas de México con alto riesgo de transmisión de TB en pacientes con VIH

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Contexto: La posibilidad de infección por tuberculosis en pacientes con VIH, es mayor cuando la incidencia anual de TB bacilifera en el comunidad, es elevada.

Metodología: Se identificaron los municipios con incidencia de 25 o más casos de tuberculosis bacilifera × 100 mil habitantes del año 2009, a los cuales se les denominó de alto riesgo y se compararon los resultados con la incidencia anual de casos TB-VIH.

Resultados: 85 municipios con tasa anual mayor a 25 × 100 mil, 5 de los cuales reportan tasas mayores a 100 casos × cada 100 mil hab. Algunos Estados con tasas de TB-VIH de 1.1 a 2.5 × 100 mil habitantes guardan correspondencia con el grupo identificado como de alto riesgo.

Conclusiones: La identificación de municipios de alto riesgo de infección anual que aún no presentan tasas elevadas de TB-VIH, permite dirigir a áreas, la quimioprofilaxis y medidas preventivas en pacientes con VIH.

PS-100746-15   Achieving an impact on TB rates in the Pacific

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Background and challenges to implementation: The Pacific region is made up of 22 island countries and territories with diverse populations, cultures, economies and politics. The internationally recommended DOTS strategy was introduced in the region in 1998 and since this time, DOTS has been implemented in all Pacific countries with the exception of 2 small island states. Implementation has been challenging due to the Pacific geography (7500 islands spread over 30 million square kilometres) and differing burdens of TB, with some countries reporting extremely high rates (i.e. above 300/100 000 population) and others reporting few cases of TB.

Intervention: The DOTS strategy has been implemented incrementally in the Pacific region since 1998. Recently, modeling of impact indicators was carried out by SPC, based on WHO estimates. Two of the key impact indicators (prevalence and mortality) were calculated to determine the long term impact of DOTS and assess progress towards 2010 regional targets.

Results and lessons learned: In the Pacific, between 2000 and 2010, the estimated TB prevalence decreased by 42.8% (excluding PNG) at an average of 5.6% per year. The prevalence rate has fallen from 484/100 000 in 2000 to 398/100 000 in 2010. The estimated mortality decreased by 39.8% in the same time period, at an average of 5.1% per year. The mortality rate has fallen from 13/100 000 in 2000 to 8/100 000 in 2010. The targets for the region were to reduce TB related prevalence and mortality by half by 2010 relative to the levels in 2000. These targets were narrowly missed.

Conclusions and key recommendations: The DOTS strategy has now been implemented for 13 years in the Pacific in countries with significant geographical and epidemiological challenges. TB related prevalence and mortality are steadily being reduced and the 2010 targets were narrowly missed. Intensified efforts may be needed in selected countries to meet the 2015 international targets.

PS-100295-15   Burden of tuberculosis and health seeking behaviours of people with prolonged cough in rural PNG

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Setting: Rural communities in SumKar district, Madang Province.

Objective: To determine the actual prevalence rate of TB illness compared with the TB rate detected by 'passive case finding' approach and to investigate the delay of seeking health care and diagnosis. And to explore and investigate health seeking behaviour of prolonged cough patients.

Design: A house to house survey was carried out to identify prolonged cough cases and sputum specimens were tested for TB with Acid Fast bacilli (AFB) microscopy. Questionnaire survey was carried out to explore health seeking behaviour.

Results: A total of 184 of 7211 people reported prolonged cough and 19 new TB cases were detected. Passive case finding detected only 40% of all new TB case. Approximately 40% of TB cases had never sought any forms of health centre. Those seeking health care, sought within 16 days after onset of cough. Diagnosis delay, however, was pronounced with overall median delay of 12 months. Most of respondents had limited knowledge of causes and TB transmission. Better knowledge was significant related to the educational levels; however, such knowledge did not translate to better health seeking behaviour. Distance

to travel to the health centre and the severity of clinical conditions were significant factors for promptly seeking health care at health centers.

Conclusion: To achieve TB detection rate of 70%, TB control program will need to integrate active case finding approach and improving TB diagnosis in rural health level. Limited knowledge about TB and low utility of health care services indicated the need for comprehensive health education for TB that encourages appropriate health seeking behavior.

PS-101200-15   Explorative study on epidemiology and prevention of tuberculosis in isolated islands of Indonesia

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Aim: Tuberculosis is still the most health problem in Indonesia, particularly on isolated areas and remote islands. The implementation of National Tuberculosis Programme (NTP) remains low (i.e. other infectious diseases programme) in 29 islands in Flores sea including Liukang Tangaya subdistrict, Pangkep District, South Celebes Province and also other islands at Kalmas subdistrict. The purpose of this operational research is to review the existing TB programme planning and implementation on dispersed remote islands.

Methods: Active survey and structured questionnaires were administered to patients suspect TB and providers' in-charge of TB clinics from isolated islands. The outcome measure was NTP parameters, validated using PCR and compared with clinical finding. All data were analyzed by using EPI-Info version 6.02 and and clustering effect by GIS.

Results: By this research, our results are:
- Implementation of TB program on Liukang Tangaya island is not work as not as expected
- The TB prevalence rate in Liukang Tangaya island is still higher (endemic)
- The rate of failed TB treatment patients is still high due to transportation obstacles, economic problems and lack of TB medicine supplies
- The sensitivity of the Acid fast staining method is lower than culture and PCR assay
- Measurement of TB infection rate in the corresponding island populations is impossible to be performed because no measurement on its population serologic prevalence
- There is a big gap on TB knowledge between community and Health worker
- It is not possible to measure the sensitivity of microscopic assay done by Primary health centre (PUSKESMAS) worker because there is no special health worker for TB in the islands
- Distribution of cluster TB suspect in the island can be showed by GIS

Conclusion: It is recommended that a new formulation in strategy and application of TB program should be established.

PS-100259-15   Trends of tuberculosis related deaths in SAARC region

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Aim: Tuberculosis is among the top 10 causes of deaths worldwide, and one of the United Nations' Millennium Development Goals is to halve TB mortality per head by 2015, compared with 1990 levels. TB mortality is an important indicator of the success of TB control, as most of the TB burden, as measured in disability-adjusted life–years (DALYs), is the result of premature deaths among young adults. The aim of the study was to describe trend of TB related deaths in SAARC region from 2000 to 2007.

Methods: A record based descriptive study was carried out. Data was collected from the World Health Organization–Global TB control reports and Annual Reports of SAARC member states which were published from 2000 to 2008.

Results: Mortality rates due to TB have been reduced over the years (from 2000 to 2007) in all the SAARC member states. In year 2007, highest death rate was reported in Bhutan (44 per 100 000 population) and lowest rates reported from Maldives (4 per 100 000 population) and Sri Lanka (8 per 100 000 population).

Conclusion: By adopting DOTS strategy, this region has started to show success in TB control with the achievement of global target of 85% treatment success rate of new smear positive cases and reducing the mortality rates. MDR-TB and HIV/AIDS are the main hurdles for TB control. The member states need to focus their attention to strengthen management of MDR-TB and HIV associated TB to further reduce the TB related mortality.

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