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## Operational assessment of novel tools for rapid diagnosis of MDR-TB in resource-poor settings

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**Background** - Sputum smear microscopy is enshrined in the DOTS strategy for global TB control as the diagnostic test of choice because it is cheap, simple and detects the most infectious cases. Sputum culture and susceptibility testing are the standard of care in industrialized countries because early, accurate diagnosis of TB and MDRTB reduces morbidity, mortality and interrupts transmission. However, access to such diagnostics is rarely available in resource-limited settings where the burden of TB is highest and the need for novel practical tools most urgent. Rapid, sensitive detection of TB/MDRTB direct from sputum has been demonstrated in proof-of-principle studies of the microscopic observation drug susceptibility assay (MODS). We sought to determine whether the "real-world" performance of MODS would make it suitable for wider implementation.

**Methods**-We evaluated, in an operational setting in Peru, the performance of MODS amongst three target groups: unselected TB suspects, high-risk TB/MDRTB suspects and unselected hospitalized HIV patients. The detection sensitivity, speed, contamination rate and reliability of direct susceptibility testing in MODS was compared head-to-head with the dual gold-standards of automated MBBacT culture and susceptibility testing and Löwenstein Jensen (LJ) culture with proportion method susceptibility testing.

**Findings**-401 of 3760 sputum samples (10.7%) yielded positive *M tuberculosis* cultures. Detection sensitivities for MODS, MBBacT and LJ were 97.8%, 89.0% and 84.0% respectively ( $p < 0.001$ ). One sputum culture, regardless of method, was significantly superior to two sputum smears - incremental benefit of a second culture was small.

Median time [IQR] to culture-positivity was 7 [6-8], 13 [10-16] and 26 [21-33] days ( $p < 0.0001$ ). MODS drug susceptibility results were available on the same day as cultures were positive. Direct susceptibility testing demonstrated proportion agreements of 100%, 97%, 99%, 95% and 92% for rifampicin, isoniazid, MDR, ethambutol and streptomycin respectively (kappa values - 1.0, 0.89, 0.93, 0.71, 0.72).

**Interpretation**-A single MODS sputum culture (costing  $< \$2$ ) offers rapid, sensitive and reliable detection of TB and MDRTB. The opportunity to interrupt transmission and provide equitable access to TB diagnostic testing in high-burden, resource-limited settings is now available and large scale demonstration projects with cost-effectiveness analyses and process evaluation are warranted.

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