

## Evidence-based Tuberculosis Diagnosis

One-page plain language summaries of systematic reviews - #6

### Title: MODS and TLA assays for detection of drug resistant TB

This *systematic review* presents *evidence* from a collection of studies evaluating tests or strategies for the diagnosis of tuberculosis (TB). Terms in *italics* are defined in the TB Evidence Glossary.

**Why this review is important:** Resistance to first line TB drugs has complicated treatment considerably and become a major obstacle to global TB control. Multidrug-resistant TB (MDR-TB) is defined as resistance to at least isoniazid and rifampicin, the 2 best first-line drugs used to treat TB. Extensively drug-resistant (XDR) TB is a relatively rare form of MDR-TB with resistance to almost all drugs used to treat TB, including isoniazid and rifampicin, and the best second-line drugs: fluoroquinolones and at least 1 of 3 injectable drugs. In 2008, there were an estimated 440,000 cases of MDR-TB, but only approximately 10% of these patients received a diagnosis. The high mortality associated with MDR-TB and XDR-TB, especially in patients with HIV co-infection, has highlighted the urgency for rapid screening for drug resistance. Several methods to detect drug resistance, of varying complexity, time to results, cost, and laboratory requirements, are available. The 2 noncommercial methods evaluated in this systematic review, microscopic-observation drug susceptibility (MODS) and thin-layer agar (TLA) assays are quick, inexpensive, and relatively easy to do, making these methods useful for resource-limited settings.

**Objective:** to determine the *sensitivity* and *specificity* of MODS and TLA assays for detection of TB drug resistance. To combine results from individual studies in a meta-analysis to obtain summary (pooled) estimates for sensitivity and specificity.

**Main findings:** 12 studies (9 for MODS and 3 for TLA assays) were included in the review. MODS: for detection of rifampicin resistance, pooled sensitivity estimate was 98% (95% CI 95,99) and pooled specificity estimate 99% (96,100); for detection of isoniazid resistance, pooled sensitivity was slightly lower depending on the drug concentration used for testing. TLA assay: pooled sensitivity and specificity estimates for resistance to rifampicin (3 studies) and isoniazid (2 studies) were 100%. Time for results was 10 days for MODS and 11 days for TLA assay.

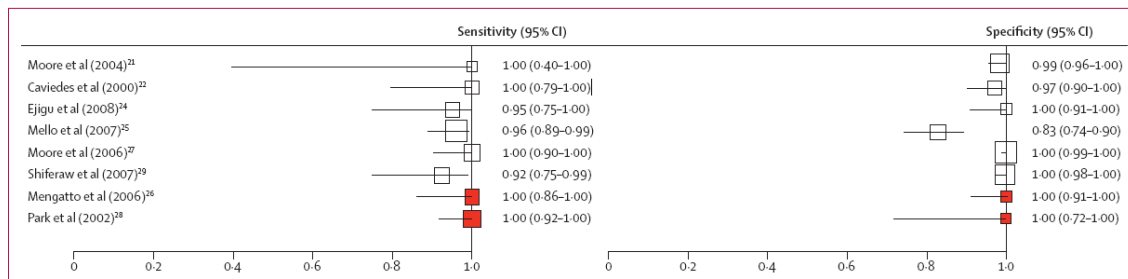


Figure 2: Forest plot of accuracy of the microscopic-observation drug susceptibility assay for rifampicin resistance

Open squares represent studies using direct inoculation with specimens from patients; red squares represent studies using indirect inoculation with isolates. Size of the square is proportionate to the size of the study.

**Authors' conclusions:** MODS shows high sensitivity when testing for rifampicin resistance, but slightly lower sensitivity when testing for isoniazid resistance. There are few studies evaluating the TLA assay for the detection of drug susceptibility; however, all studies to date have found 100% accuracy.

**Policy implications:** In 2009, WHO recommended that selective noncommercial methods be used as an interim solution in resource-constrained settings for culture and detection of drug resistance while capacity for more advanced systems were being developed. MODS received an endorsement with the qualification that this method be used under clearly defined programmatic and operational conditions and after concerns about mycobacterial speciation and biosafety were addressed.

**Comments:** WHO felt that the current evidence on TLA assays was insufficient to recommend their use.

**Systematic review:** Minion J et al. Microscopic-observation drug susceptibility and thin layer agar assays for the detection of drug resistant tuberculosis: a systematic review and meta-analysis. *Lancet Infect Dis.* Oct;10(10):688-98. Available at [www.tbevidence.org](http://www.tbevidence.org)

### Publications and other resources of related interest

1. Moore DA et al. Microscopic-observation drug-susceptibility assay for the diagnosis of TB. *N Engl J Med.* 2006 Oct 12;355(15):1539-50. 2. Minion J, Pai M. Expanding the role of the microscopic observation drug susceptibility assay in tuberculosis and HIV management. *Clin Infect Dis.* Apr 1;50(7):997-9 3. Noncommercial culture and drug-susceptibility testing methods for screening patients at risk for multidrug resistant tuberculosis

[http://www.who.int/tb/laboratory/whopolicy\\_noncommercialculture\\_and\\_dst\\_methods\\_mar2011.pdf](http://www.who.int/tb/laboratory/whopolicy_noncommercialculture_and_dst_methods_mar2011.pdf)

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