Evidence-based Tuberculosis Diagnosis
One-page plain language summaries of systematic reviews - #8

Title: GenoType MTBDR, a line-probe assay for the diagnosis of multidrug-resistant tuberculosis
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. Conventional methods for mycobacterial culture and drug susceptibility testing (DST) are slow and complex. Therefore, attention has turned to line-probe assays which detect genetic sequences associated with resistance. GenoType MTBDR is a line-probe assay (Hain LifeScience GmbH, Nehren, Germany) that can detect both rifampicin and isoniazid resistance.

Objective: To determine the accuracy of GenoType MTBDR assays for diagnosing MDR-TB in cultures and clinical specimens. To combine results from individual studies in a *meta-analysis* to obtain summary (pooled) estimates for *sensitivity* and *specificity*.

Main findings: 10 papers were included in the review, including 14 comparisons for the detection of rifampicin resistance and 15 comparisons for the detection of isoniazid resistance. With GenoType MTBDR plus, the newest version of the assay, pooled sensitivity and specificity for rifampicin resistance was very high: 98% (95,100) and 99% (97,100), respectively The pooled sensitivity for isoniazid resistance was lower than that for rifampicin resistance, 89% (82,93), but specificity was high 99% (95,100). Results were excellent for cultures, as well as clinical specimens.

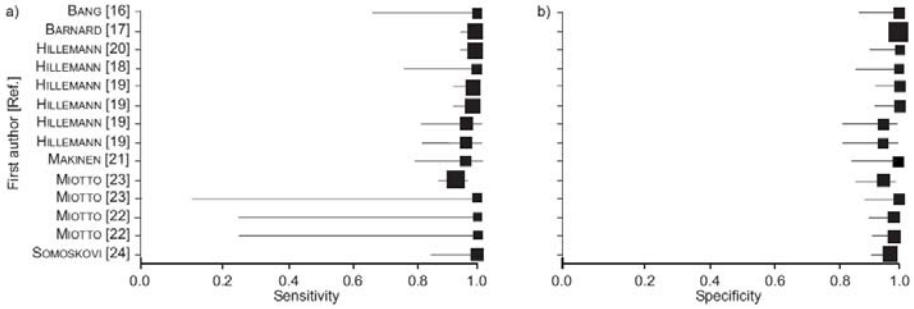

Figure. Forest plot of sensitivity (a) and specificity (b) estimates for rifampicin resistance; squares show point estimates of sensitivity and specificity from each study; 95% CIs are shown by the horizontal lines.

Authors' conclusions: GenoType MDTBR assays demonstrate excellent accuracy for rifampicin resistance, which is a proxy for MDR-TB. This suggests good utility as a rapid screening tool, especially in settings with high rates of MDR-TB or HIV and where infection control is a major concern.

Policy implications: In 2008, WHO endorsed the use of line probe assays stating: Adoption of line probe assays for rapid detection of MDR-TB should be decided by Ministries of Health within the context of country plans for appropriate management of MDR-TB patients, including the development of country-specific screening algorithms and timely access to quality-assured second-line anti-TB drugs.

Comments: The recommended use of line-probe assays is currently limited to culture isolates and direct testing of smear-positive sputum specimens. Line-probe assays are not recommended as a complete replacement for conventional culture and drug susceptibility testing.

Systematic review: Ling DI, Zwerling AA, Pai M. GenoType MTBDR assays for the diagnosis of multidrug-resistant tuberculosis: a meta-analysis. Eur Respir J. 2008 Nov;32(5):1165-74. Available at www.tbevidence.org

Publications and other resources of related interest

1. Molecular line probe assays for rapid screening of patients at risk of multidrug-resistant tuberculosis: WHO policy statement. http://www.who.int/tb/features_archive/policy_statement.pdf

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