

Title: Urine lipoarabinomannan for the diagnosis of 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: The detection of lipoarabinomannan (LAM), a major glycolipid component of the cell wall of *M. tuberculosis* and other mycobacteria, is a potential approach to diagnosing active TB. LAM can be detected in urine. Urine is a particularly appealing clinical specimen for diagnosis because urine is simple to obtain in adults and children (young children may have difficulty producing sputum) and can be easily processed and stored. In addition, a urine specimen presents low risk of infection to health care workers and could be tested in health centers with limited laboratory facilities. Could urine LAM be the point-of-care test we are hoping for?

Objective: to determine the *sensitivity* and *specificity* of urine LAM antigen detection for the diagnosis of active TB. To combine results from individual studies in a *meta-analysis* to obtain summary (pooled) estimates for sensitivity and specificity.

Main findings: 9 studies were included in the review. Using culture or microscopy smear as the *reference standard* (7 studies), urine LAM sensitivity estimates for individual studies ranged from 13% to 93% and specificity estimates from 87% to 99%. In the meta-analysis, pooled sensitivity in HIV-infected individuals was 56% (95% CI 40, 71) and in HIV-uninfected individuals, pooled sensitivity was 18% (95% CI 10, 29); pooled specificities were 95% (95% CI 77, 90) and 90% (95% CI 85, 93), respectively. In the 5 studies with information on HIV infection, sensitivity was 3% to 53% higher in the HIV-infected than the HIV-uninfected groups with the highest sensitivity reported in HIV-infected individuals with advanced immunosuppression.

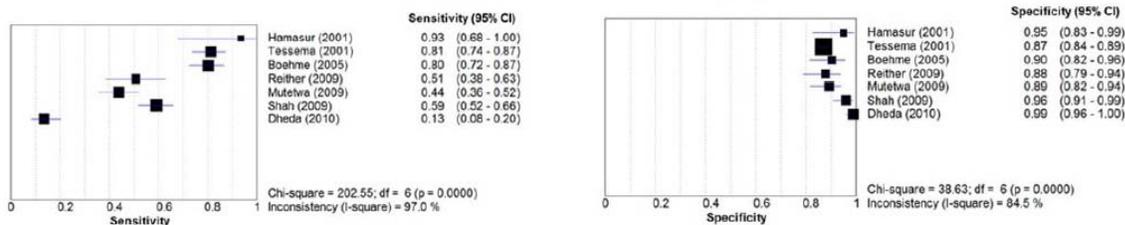


Figure. Forest plots of urine LAM sensitivity and specificity; squares show point estimates of sensitivity from each study; 95% CIs are shown by the horizontal lines.

Authors' conclusions: Although urine LAM has several characteristics that make it potentially useful as a test for active TB, the systematic review found sensitivity to be low. Urine LAM is not recommended as a routine test for the diagnosis of active TB in patients with TB symptoms. Urine LAM performs better in HIV-infected patients with suspected active TB, especially those individuals with advanced immunodeficiency.

Policy implications: WHO has not issued a policy recommendation about urine LAM.

Comments: Urine LAM was originally considered to be a potential breakthrough for the diagnosis of active TB because of its potential to be used as a simple point-of-care test. Despite initial promising results, more recent studies have failed to demonstrate adequate sensitivity for TB diagnosis for patients being evaluated in routine conditions. Newer versions of LAM are becoming available and these versions may have improved performance.

Systematic review: Minion J, Leung E, Talbot E, Dheda K, Pai M, Menzies D. Diagnosing tuberculosis with urine lipoarabinomannan: systematic review and meta-analysis. *Eur Respir J.* 2011 Jul 4

Publications and other resources of related interest

1. Peter J, Green C, Hoelscher M, et al. Urine for the diagnosis of tuberculosis: current approaches, clinical applicability, and new developments. *Curr Opin Pulm Med.* 2010 May;16(3):262-70. 2. Lawn SD, Edwards DJ, Kranzer K, et al. Urine lipoarabinomannan assay for tuberculosis screening before antiretroviral therapy diagnostic yield and association with immune reconstitution disease. *AIDS.* 2009 Sep 10;23(14):1875-80.

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