

## Evidence-based Tuberculosis Diagnosis

One-page plain language summaries of systematic reviews - #4

### Title: Commercial Nucleic-Acid Amplification Tests for the Diagnosis of Pulmonary 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:** Nucleic acid amplification (NAA) tests isolate, replicate, and detect nucleic acid sequences specific for *Mycobacterium tuberculosis*. NAA tests were developed to aid in the rapid diagnosis of active TB. NAA tests can reliably detect TB bacteria in specimens in 24-48 hours compared with culture which may take 2-6 weeks for results. Earlier diagnosis may lead to earlier treatment, less severe illness, decreased mortality, and decreased spread of TB. Commercial NAA tests have been shown to give more consistent results than noncommercial NAA tests.

**Objective:** To determine the accuracy of commercial NAA tests to diagnose pulmonary TB and, in addition, to identify factors associated with higher or lower test accuracy. To combine results from individual studies in a *meta-analysis* to obtain summary (pooled) estimates for *sensitivity* and *specificity*. To explore reasons for *heterogeneity* (*inconsistent* results) among the studies.

**Main findings:** 125 studies from 105 papers were included. The majority of studies were observational studies of patients suspected of having TB. The pooled sensitivity was 85% (range 36% to 100%) and the pooled specificity 97% (range 54% to 100%) with wide ranges, meaning the results were inconsistent. The use of different cut-off values for test positivity and the use of specimens other than sputum could explain some of the observed heterogeneity.

**Table. Sensitivity and specificity of 125 nucleic acid amplification test studies**

Accuracy Measure	Accuracy Estimate (95% Confidence Interval)	Chi <sup>2</sup> test of heterogeneity	P value for heterogeneity
Sensitivity	85% (85, 86)	1121.69	< .001
Specificity	97% (97, 97)	3748.64	< .001

**Authors' conclusions:** Commercial NAA tests alone cannot be recommended to replace conventional tests such as mycobacterial culture for diagnosing pulmonary TB. Improvements in diagnostic accuracy, particularly sensitivity, need to be made in order for this expensive technology to be worthwhile and beneficial in low-resource countries.

**Policy implications:** WHO has not issued a policy on the use NAA tests for active TB.

**Comments:** Two NAA tests are approved by the US Food and Drug Administration: enhanced MTD test (Gen-Probe, San Diego, California) is approved for use for both smear-positive and smear-negative respiratory specimens and the Amplicor Mycobacterium tuberculosis Test (Roche Diagnostics, Basel, Switzerland) is approved for use for smear-positive respiratory specimens. The US Centers for Disease Control and Prevention recommends that NAA testing should be performed on at least one respiratory specimen from each patient with signs and symptoms of pulmonary TB for whom a diagnosis of TB is being considered but has not yet been established, and for whom the test result would alter case management or TB control activities.

**Systematic review:** Ling DI, Flores LL, Riley LW, Pai M (2008) Commercial Nucleic-Acid Amplification Tests for Diagnosis of Pulmonary Tuberculosis in Respiratory Specimens: Meta-Analysis and Meta-Regression. PLoS ONE 3: e1536. Available at [www.tbevidence.org](http://www.tbevidence.org)

#### Publications and other resources of related interest

1. Centers for Disease Control and Prevention (CDC). Updated guidelines for the use of nucleic acid amplification tests in the diagnosis of tuberculosis. MMWR Morb Mortal Wkly Rep 2009;58:7-10.
2. Dorman S. Coming-of-age of nucleic acid amplification tests. Clinical Infectious Diseases 2009; 49:55-7

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