Evidence-based Tuberculosis Diagnosis
One-page plain language summaries of systematic reviews - #15

Title: Predictive value of interferon-gamma release assays for active tuberculosis
This systematic review presents evidence from a collection of studies evaluating tests that predict the development of active tuberculosis (TB). Terms in italics are defined in the TB Evidence Glossary.

Why this review is important: Most people infected with TB never get TB symptoms. This is called latent TB infection (LTBI). The tuberculin skin test (TST) has traditionally been used to diagnose LTBI. TST positivity is a surrogate marker for risk of developing active TB (with those testing positive having a relative risk of about two), and TST-positive individuals benefit from isoniazid preventive treatment. Interferon-gamma release assays (IGRAs) are blood tests that were recently developed as alternatives to the TST to aid in the diagnosis of LTBI. Among people with LTBI, what do the data reveal about the ability of IGRAs to predict the development of active TB?

Objective: To assess whether IGRAs can predict the development of active TB in individuals without active disease at baseline and to determine whether IGRA predictive ability is higher than that of TST. Results from individual studies were combined in a meta-analysis to obtain summary (pooled) estimates for rates of progression to TB disease measured by incidence rate ratios (IRR) in IGRA-positive versus IGRA-negative and TST-positive versus TST-negative participants.

Main findings: 15 studies (26,680 participants) were included in the review; 9 studies were from low/middle-income countries and 6 studies from high-income countries. The median study period was 4 years. Compared with test-negative results, IGRA-positive and TST-positive results were similar with respect to the risk of developing active TB: pooled IRR in the five studies that used both IGRA and TST was 2.11 (95% CI 1.29, 3.46) for IGRA versus 1.60 (95% CI 0.94, 2.72) for TST (at the 10 mm cutoff).

Authors’ conclusions: The strength of the association between IGRA-positive results and development of active TB in the studies was modest, with relative risks of about 2 to 3. Hence, the most important finding in this review is that none of the commercially available tests for LTBI have high predictive value. The decision to choose one test (IGRA or TST) over another should be based on specificity, logistics, cost, and patient preference.

Policy implications: In September 2010, the WHO’s Strategic and Technical Advisory Group for TB (STAG-TB) decided to discourage the use of IGRAs for the diagnosis of active TB and LTBI in low-income and middle-income countries (typically high-TB and/or high HIV prevalence settings).

Comments: Further research is needed to identify predictive biomarkers for tests for LTBI. The revised Global Plan to Stop TB (2011–15) has set a goal for such tests.

Systematic review: Rangaka M, Wilkinson K, JR Glynn, et al. Predictive value of interferon-gamma release assays for incident active tuberculosis: A systematic review and meta-analysis. The Lancet Infectious Diseases, In press.

Publications and other resources of related interest
1. The Global Plan to Stop TB [http://www.stoptb.org/global/plan/]. 2. Comstock GW, Livesay VT, Woolpert SF. The prognosis of a positive tuberculin reaction in childhood and adolescence. Am J Epidemiol. 1974; 99(2): 131-8.

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"Incidence rate ratio (IRR) is the ratio of two incidence rates. The incidence rate is a measure of the frequency with which an event, such as a new case of illness, occurs in a population over a period of time (also called person-time incidence rate).

"Biomarker can be defined as a characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention.” US National Institutes of Health