Title: Interferon-gamma release assays for pulmonary tuberculosis in low- and middle-income countries
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: Interferon-gamma release assays (IGRAs) are blood tests that were recently developed as alternatives to the 100 year-old tuberculin skin test (TST) to aid in the diagnosis of latent TB infection (LTBI). IGRAs are mainly used to diagnose LTBI in high-income countries, but are increasingly being used to diagnose active TB in low-income and middle-income countries. Two IGRAs are in current use: QuantiFERON® - TB Gold In-Tube (QFT-GIT), Cellestis Limited, Victoria, Australia and T-SPOT®.*TB* (TSPOT), Oxford Immunotec, Abingdon, UK.

Objective: To determine the *sensitivity* and *specificity* of IGRAs for the diagnosis of pulmonary TB in adults in low- and middle-income countries. To combine results from individual studies in a *meta-analysis* to obtain summary (pooled) estimates for sensitivity and specificity.

Main findings: 27 studies (TSPOT 10 studies; QFT-GIT 17 studies) involving 590 HIV-uninfected and 844 HIV-infected individuals were included in the review. Among people with HIV-infection, pooled sensitivity estimates were modest: TSPOT 76% (95% CI 45,92; 4 studies); QFT-GIT 60% (95% CI 34,82; 5 studies). Among people without HIV-infection, pooled sensitivity estimates were higher: TSPOT 88% (95% CI 81,95; 4 studies); QFT-GIT 84% (95% CI 78,91; 9 studies).The specificity of both IGRAs was low (< 65%), regardless of HIV status.
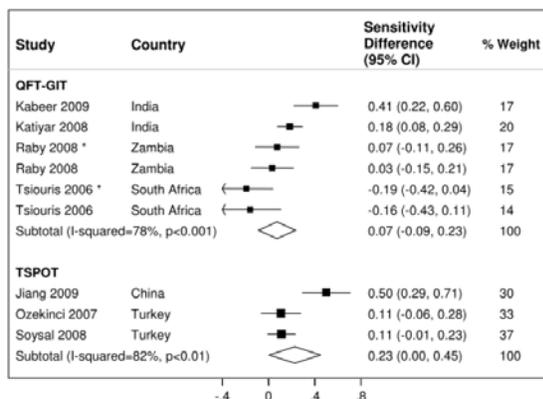

Figure. Percent sensitivity difference between IGRA and TST results. Squares show point estimates of sensitivity difference from each study and diamonds the pooled sensitivity estimates; 95% CIs are shown by the horizontals lines. There was no consistent evidence that either IGRA was more sensitive than the TST for the diagnosis of active TB.

Authors' conclusions: As is the case for TST, there is no role for using IGRAs for the diagnosis of pulmonary TB in adults in low-income and middle-income countries, especially in high HIV settings.

Policy implications: In September 2010, the Strategic and Technical Advisory Group (STAG-TB) acknowledged the large body of work and compelling evidence demonstrating the poor performance of current commercial IGRAs in low- and middle-income countries (typically high-TB and/or high HIV settings) and the adverse impact of mis-diagnosis and wasted resources on patients and health services when these tests are used for diagnosis of active TB.

Systematic review: Metcalfe JZ et al. Interferon-gamma release assays for active pulmonary TB diagnosis in adults in low- and middle-income countries: Systematic review and meta-analysis. J Infect Dis 2011, in press.

Publications and other resources of related interest
1. Ling DI, et al. Are interferon-{gamma} release assays useful for active tuberculosis in a high-burden setting? Eur Respir J. Feb 24. 2. Menzies D. Using tests for latent tuberculous infection to diagnose active tuberculosis: can we eat our cake and have it too? Ann Intern Med 2008;148:398-9 3. STAG-TB http://www.tbevidence.org/documents/policies/stag_tb_report_2010.pdf

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