

Evidence-based Tuberculosis Diagnosis

One-page plain language summaries of systematic reviews - #9

Title: Interferon-gamma release assays for active tuberculosis and latent tuberculosis infection in children

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: Over one million children develop TB every year with the vast majority of cases occurring in low-and middle-income countries. Young children have a particularly high risk of developing active TB following infection, and are more likely to develop severe forms of disease, such as TB meningitis and disseminated TB. Children with latent tuberculosis infection (LTBI) could benefit considerably from treatment to prevent the development of active TB. Treatment for LTBI in low-and middle-income countries is mainly given based on the presence of risk factors, such as young age and HIV, since tests to diagnose LTBI, like the tuberculin skin test (TST), have shortcomings, particularly in BCG-vaccinated and HIV-infected children. The newly developed interferon-gamma release assays (IGRAs) could be an option for detection of active TB and LTBI. Two IGRAs are in current use: Cellestis Limited, Victoria, Australia and T-SPOT®.TB (TSPOT), Oxford Immunotec, Abingdon, UK and QuantiFERON® -TB Gold In-Tube (QFT). Studies using an older version of QuantiFERON were also included in this review.

Objective: to assess the performance of IGRAs and TST for the diagnosis of active TB and LTBI in children. To combine results from individual studies in a *meta-analysis* to obtain summary (pooled) estimates for *sensitivity* and *specificity*.

Main findings: 32 studies involving 4122 children were included in the analyses. The average age of the children was 8 years; BCG vaccination ranged from 8% to 100%. In low- and middle-income countries, the pooled sensitivity of IGRAs for detecting active TB was 77% (TSPOT) and 58% (QFT); specificity was 93% (TSPOT) and 94% (QFT). Only 2 small studies from high-income countries were identified that prospectively estimated active TB incidence in children who had been tested with QFT; results were conflicting. When the *reference standard* for LTBI was exposure, all 3 tests (TST, QFT, and TSPOT) were associated with exposure; however, differences in methods concerning the reference standards for active TB and definitions of exposure made it difficult to compare results among studies. The review found no difference in performance between TST and IGRAs for the diagnosis of active TB and LTBI in children. Both IGRAs and TST showed lower sensitivity in HIV-infected children.

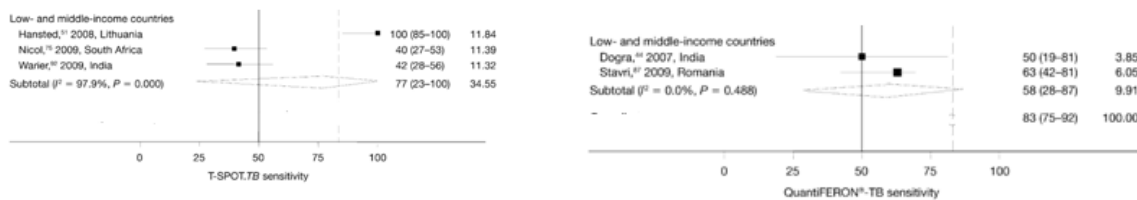


Figure. Forest plots of TSPOT and QFT sensitivity for active TB; squares show point estimates of sensitivity from each study; diamonds show pooled estimates; 95% CIs are shown by the horizontal lines.

Authors' conclusions: TST, QFT and TSPOT had similar accuracy for the diagnosis active TB and LTBI in children.

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 children living in low-income and middle-income countries, irrespective of HIV status..

Comments: The authors commented that more high-quality diagnostic studies are needed to inform recommendations regarding IGRA use in very young and HIV-infected children, 2 groups with the highest risk of developing active TB following infection.

Systematic review: Mandalakas AM, Detjen AK, Hesselning AC, Benedetti A, Menzies D. Interferon-gamma release assays and childhood tuberculosis: Systematic review and meta-analysis. Int J Tuberc Lung Dis 2011 July. doi:105588/ijtld100631 Available at www.tbevidence.org

Publications and other resources of related interest

1. Cruz AT, Starke JR. Pediatric tuberculosis. *Pediatr Rev*.2010 Jan;31(1):13-25. <http://pedsinreview.aappublications.org/cgi/reprint/31/1/13>
2. STAG-TB http://www.tbevidence.org/documents/policies/stag_tb_report_2010.pdf

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