Evidence review: Effectiveness of TB blood testing as a replacement for TB skin testing

The recent publication of the largest-ever US study comparing the use of TB blood tests (IGRAs) to the tuberculin skin test (TST) reaffirms current guidance regarding the preferred use of IGRAs for at-risk populations (1). Including more than 20,000 participants across 10 US sites, the landmark Tuberculosis Epidemiologic Studies Consortium (TBESC) study demonstrates that TB blood testing more accurately identifies latent TB among non-US-born individuals that have received the BCG vaccination, compared to TST.

TBESC overview

TBESC is a US CDC-funded collaboration between US academic centers and public health partners, which has conducted a large-scale, longitudinal study in which the authors sought to examine:

- Results agreement between TST and IGRA
- Potential ability of TST and IGRAs to accurately predict progression of latent TB infection to active TB disease, both overall and in key subgroups
- Application of accordance and discordance to provide guidance on applicable use of TST and IGRA in key subgroups

Patients enrolled in the TBESC study represent a broad scope of age categories (<2 years to >65 years old), nationalities, and US CDC-identified high-risk populations including close TB contacts, immuno-compromised, and homelessness. Study participants receieved a TST and two IGRAs upon enrollment, and were followed up after two years for development of TB disease and through state registry matches throughout the study observation period.

Authors' key finding: results agreement

The TBESC study found that positivity for latent TB infection among non-US-born people was 24% for IGRAs versus 43.2% for the TST, representing a false positivity with the TST that may prove costly and inefficient in a healthcare setting. Importantly, this discordance persisted across all reported age groups and supports existing recommendations by numerous professional organizations to use IGRA testing in place of TST for high-risk individuals.

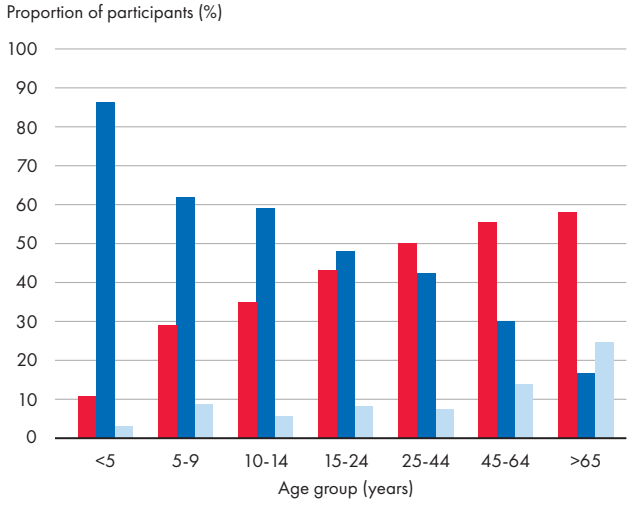

Figure 1: Test result combinations for non-US-born participants with at least one positive test separated by age group.

Considering the data generated through the TBESC study, the authors acknowledge the logistical benefits of implementing a more specific TB test instead of the TST. "The use (of IGRAs) will reduce overdiagnosis and allow public health programs to effectively focus their scarce resources."

Authors' key finding: predicting progression

The authors report that the TBESC data reflects the findings of earlier, smaller prospective studies confirming the potential opportunity for IGRAs to positively and negatively predict progession of latent infection to active TB disease. "Given the increased specificity of IFN-γ release assays, their use could translate into fewer radiographic studies and clinical evaluations and less latent tuberculosis infection treatment."

Authors' key finding: guidelines and recommendations

The authors cite two existing US CDC recommendations that are reaffirmed through TBESC findings (2):

1) High-risk individuals should receive a TB test

- Individuals from countries with a high TB prevalence
- Close contacts of active tuberculosis cases
- People with immune-suppressive conditions due to disease or medication

2) IGRA testing is preferred over the TST for non-US-born indivuduals

Additional TBESC study findings:

The authors found the QuantiFERON indeterminate rate to be 0.4% in the study population.

Significance: *Only a small number patients require retesting due to indeterminate results, maintaining the efficiency of an IGRA strategy.*

Discordance between TST and IGRA was highest in patients under the age of 5.

Significance: *Due to the proximity of BCG vaccination in non-US-born small children, TST is ineffective at identifying true latent TB infection.*

Proportions of positive IGRA results increased with age in the non-US-born population, correlated to a longer length of time for opportunity of exposure.

Significance: *Foreign-born individuals from high-incidence countries that move to the US in older years may represent a higher risk for latent TB.*

The landmark TBESC study delivers a clear message that proactive TB testing of high-risk individuals – particularly those at risk of exposure (close contacts, non-US-born) or progression (immune-compromised) – is warranted and encouraged. Use of an IGRA in place of TST will further enhance the effectiveness and efficiency of modern TB screening programs.

References:

1. Ho, C.S. et al. (2021) Comparison of three tests for latent tuberculosis infection in high-risk people in the USA: an observational cohort study. Lancet Infect Dis. doi.org/10.1016/S1473-3099(21)00145-6.
2. Lewinsohn, D.M. et al. (2017) Official American Thoracic Society/Infectious Diseases Society of America/Centers for Disease Control and Prevention Clinical Practice Guidelines: Diagnosis of Tuberculosis in Adults and Children. Clin. Infect. Dis. 64, 111-115.