Major Compulsory Revisions

General comments--This is an ambitious evaluation comparing the use of QuantiFERON-TB Gold In-Tube with TST for the diagnosis of latent TB infection (LTBI) and TB disease in Warao Ameridian contacts of TB patients. While the paper presents useful data and hypotheses, it will require significant re-working for finding and conclusions to be clearer.

Specific comments

Abstract: should be clear if the comparison is the use of these tests to diagnose LTBI, TB disease, or both. If results are not statistically significant (p=0.12, they should be described as similar). Suggest adding proportions and p-values to all results.

1. Authors need to make very clear whether the outcome being compared is test performance to detect LTBI, TB disease, or both

2. Later it is clear that Venezuelan guidelines define a positive TST as 10mm, but this should be clear in the methods (as some programs use a 5mm cutoff for contacts). Also, definition of a positive and indeterminate QFT should be clearly included in the methods (e.g. under Definitions).

3. Define “negative TST”—is it 0mm of induration, or could it include results <10mm?

4. Statistical analysis: were any power calculations done in advance to determine what sample size would be required for a statistically significant difference in study population?

5. If QFT and/or TST results are used in the case definition for TB, this presents a problem for assessing their ability to predict TB disease (as the authors point out on p.9)

6. The discussion of CXR findings is also difficult to follow. Suggest more clearly defining what is meant by “TB sequelae” and other terms (either in methods or elsewhere, and not only in discussion)

7. Logistic regression—no information was really provided on how this model was constructed (and no data are shown in table form), so it is very difficult to interpret these findings
8. Discussion: several studies have now shown that QFT has poor predictive value as a longitudinal tool. As this study (along with several others cited) has a relatively small sample size (especially when not all results are available on all children over time). This is an important limitation and thus comparisons of PPV and NPV, sensitivity and specificity across studies should be interpreted with great caution

9. CXR findings of calcification and bronchiectasis. As authors point out, these may be due to other factors (e.g. histoplasmosis for calcifications). As there is no comparison group (e.g. children who were not TB contacts), these findings (and their association with TB exposure or infection) should be interpreted with caution

Minor Essential Revisions
Suggest changing “recommendable” to “recommended”

Introduction:
1. In general, the introduction is very long and should focus more on the specific comparisons of interest. Other relevant information might better fit in the discussion

2. Rapid disease progression is especially a concern in young children (less than 3 years of age), so consider adding “young”

3. Discussion of CXR findings is a bit confusing and should relate to the methods and findings of the study. Not sure if authors mean “hilar adenopathy” when they refer to “regional adenopathy”?

4. 6th paragraph, suggest changing “extraordinary” to “extraordinarily”

5. To understand potential bias in the sample, it would be useful to know if these were all child TB contacts during the time period, or what % and how many refused to participate

6. See consensus definition of childhood TB cases from NIH and whether it can be applied to these cases

7. BCG vaccination status. Not all children with documented vaccination develop a scar, particularly in settings of immunosuppression (e.g. HIV, malnutrition). Consider adding this as a limitation, as you did not examine BCG records

8. Suggest describing as TB treatment (not anti-TB)

9. Suggest avoiding the terminology t=6 or t=12, and instead writing “at six-month follow-up”, etc.

10. Suggest rephrasing as “reported or documented fever”. Methods imply that a physical exam was part of all contact investigations—this should be made clear

11. As not all tests were available on all children, it becomes difficult to follow the denominators for the results. Suggest making this clearer in the figure and in the text.

12. Suggest adding in the % of indeterminate results (e.g. for QFT)

13. Was the child with “hip bone TB” bacteriologically confirmed? If so, suggest classifying as culture positive
14. As the authors do not really describe findings related to malnutrition (other than prevalence in this population of contacts) or other immunologic parameters, the inclusion in the discussion seems out of place

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests