**Reviewer’s report**

**Title:** Interferon-γ release assay as a sensitive diagnostic tool of latent tuberculosis infection in patients with HIV: a cross-sectional study

**Version:** 0  **Date:** 25 May 2018

**Reviewer:** Harriet Mayanja-Kizza

**Reviewer's report:**

The study looked at persons with HIV most stabilized on ART, clinically classified risk for LTBI.

Issues to consider

1. Clinical definition of risk key to study, needs better presentation

   a. Lines 120 to 130

   HIGH - "Individuals at high risk for LTBI were those with a history of contact with a household member with active TB and/or contact with smear positive individuals in the past two years, associated with the following signs and symptoms observed in the index case: cough (> 3 weeks) plus at least one of the following: (a) contact with individuals who had unintentionally lost more than 10% of body weight, (b) fever (> 38 °C), and (c) night sweats."

   This is a bit unclear. What was the basis for diagnosis of active Tb in the index. Whets the relevance of contact with a person who had lost over 10% body weight among the smear positive contacts. How positive was smear positive.

   Information like smear and degree of lung disease e.g. cavities would be more useful information here.

   b. Lines 125 to 126

   LOW - "Individuals at low risk were those with a history of contact with the bacillus in the past two years only outside the household, associated with one of the signs or symptoms of the index case as above."

   How was contact outside household determined? Was this at work, school or other degree of contact. This group seems to be between the high and low risk.
c. Lines 127 to 130

LOW - "Other individuals at low risk were those with no history of contact with smear-positive individuals who also had a positive TST and those who had no history of treatment for LTBI in the last two years."

Again this is unclear. How far back was a history of a positive TST. What of those with no contact and no prior TST?

In this study, was there any difference between the 2 low risk groups - since they seem to have differing in their exposure to active TB contacts.

d. Who were the persons with "absent" risk of LTBI. Are they the ones who are double negative. if so, this is using the study results to phenotype this group.

3. Lines 221-222 "Briefly, among 80 patients who met the study criteria for LTBI (LTBI risk and at least one positive test, TST or IGRA), 59 (73.7%) were TST positive, while 21 (26.2%) were negative."

It appears a positive TST or IGRA were used to determine the LTBI risk phenotype. But then they were also used to study and compare with the clinically determined risk of LTBI. This needs clarification.

3a. In table 3 the term "absent" is not very clear. If this is clinical risk of LTBI, then its better to write "Risk for LTBI" rather than "LTBI" in table 3; this is better presented in table 4.

b. It may be a better idea if Table 3 and 4 could be combined. Then one can compare results among the high, low and absent LTBI risk.

3. Results are shown for each single test, but this does not give an indication of concordance of TST and IGRA results. One cannot tell which patients were double positive and which ones single positive. It's possible the patients positive for IGRA ,may not be the same as are positive for TST.

4. Table 3 and 4 need more clarification

Table 3. Description of frequencies related to the TST and IGRA result in 90 HIV infected patients at risk of LTBI.

Table 4. Description of frequencies related to the TST and IGRA result, according to the risk for LTBI in 90 HIV-infected patients studied.
Overall the methodology of determination and clinical classification of risk for LTBI needs better description.

It seems both clinical and either a positive TST or IGRA were included in determining clinical risk. Also the description of the TB contact was not very clear.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No.

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

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