Reviewer's report

Title: Effects of introducing Xpert MTB/RIF test on multi-drug resistant Tuberculosis diagnosis in KwaZulu-Natal South Africa

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Reviewer: Keertan Dheda

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This is a significant publication that seeks to address two issues. The first is to evaluate systems-related delay despite having the availability of a rapid diagnostic tools. The second is to study the discordance between Xpert and culture and whether confirmation of MDR-TB is required; this is a major problem in clinical practice.

Comments

1. In the abstract background section the sentence needs to be reworded as both line probe and phenotypic testing is a form of DST.

2. The confidence interval around the discordance of 8.8% needs to be stated. Same for the RIF mono resistance.

3. The key finding of the study is that a significant proportion of patients were only initiated on treatment weeks to months later despite having a rapid diagnostic tool with a turnaround time of 48 to 72 hours. The next step would to try and dissect out why this occurring? The turnaround time of the test result should be stated if possible. It should be relatively straightforward to know exactly when the sample was receipted in the lab and when the test result was generated? How was the result sent to the clinic and when was it sent?

4. I feel that the conclusion could be worded much better. Message 1 should read something like: Despite having rapid diagnostic tools like GeneXpert, failure to address systems-associated delays will result in delays in treatment initiation.

   The second key point is to point out that the discordance between Xpert and phenotypic testing is high enough to warrant DST being done.

5. The authors need to discuss this discordance issue in detail in the discussion section. The key question is if a single DST and Xpert are discordant, how does one decide whether the Xpert or the DST is correct?

6. There are a number of important publications (all done in South Africa) that have been left out and not quoted. These should be mentioned as they are directly relevant to the study and were done in South Africa. On having a quick
look: there are two papers by Theron et al. One in the AJRCCM in 2011 validates Xpert positive culture negative discordance. A second paper published in The Lancet late last year, which would shed light on some of the issues discussed here.

7. In table 1, the proportion of samples that were paired, i.e. taken together at the time the Xpert was done, should also be mentioned.

8. The authors should further suggest what recommendations arise from their findings about the delays?

For example, how should the algorithm change so as to make sure a sample is collected for potential DST should more than one sample be collected at the initial visit? In the Western Cape Province algorithms, for example, two samples are always taken. Should the RIF result be positive, then only is the second sample interrogated for DST (usually line proble) and a third sample is collected at the same time. If sample one and sample two are discordant, then DST is also done on the third sample. A final call on resistance or sensitivity is made depending on the second and the third DST (2 neg= stop MDR and follow up closely).

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

'I declare that I have no competing interests'