Reviewer's report

Title: Rapid screening of MDR-TB using molecular Line Probe Assay is feasible in Uganda

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Reviewer: Ben Marais

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Rapid screening of MDR-TB using molecular line probe assay is feasible in Uganda

The use of genotypic line probe assays for rapid drug resistance testing in sputum+ TB patients has been validated and is currently endorsed by WHO. However, additional information on its clinical implementation in TB endemic areas and performance under field conditions will help to guide more wide-scale implementation.

I offer a few comments for consideration - all are minor essential or discretionary revisions to consider. Comments follow the outline of the text/manuscript.

Title
The title accurately reflects the content of the paper.

Abstract
Accurate/good summary
1) Important to provide actual numbers and not only percentages.

Introduction
This provides sufficient background information and a clear study rationale.
2) The fact that only about 40% of new TB cases are sputum smear-positive is an important limitation of the new test in this setting, which is not adequately emphasized in the discussion.

3) Use consistent references eg. no need to refer to WHO document in brackets; mix of Roman and non-Roman numbers used.

4) Discretionary - Consider using the term “amplification of” instead of or in brackets together with “development of further” drug resistance.

Methods
This is well documented, but clarity may be improved.

5) The paragraph at the bottom of page 6 is duplicated.

6) It would be very helpful to include a schematic drawing specifying the exact
specimen flow eg. which specimens were pooled and which aliquots went where or were first frozen etc.

7) Measures taken to prevent cross contamination should be very clearly described, since this is crucial from an operational perspective.

8) Specify which MIC cut-offs were used in the conventional DST.

Results
In general the results are well presented, but clarity may be improved.

9) Reflect actual fractions not just percentages in the text.

10) Is there any indication that the mutations missed by DST are more likely to be associated with a fitness cost; therefore minor growth may not have triggered the detection signal during phenotypic testing?

11) The fact that genotypic testing missed 1/7 INH resistant specimens on DST warrants discussion, since it is not widely appreciated that INH resistance may be particularly “underdetected” given the multiple possible mutations.

12) Not only may genotypic DST provide false susceptibility results (most likely with INH as above), but rpoB wild type mutations detected by the genotypic test may be functionally silent. Was this investigated in the case where RMP resistance pattern was discrepant?

Discussion
The discussion is well-written, although it may be slightly better focused.

13) No need to repeat sensitivity and specificity figures from results section.

14) Consider adding discussion on some of the points raised under results.

15) It seems very important to clearly identify the main bottlenecks, risks and operational challenges identified during this study. Seeing that this is probably one of the most important study contributions, it may be worthwhile to summarize this in a table.

In summary
This is an important “real life study” on a very relevant topic. The results are of great public health relevance and are well presented, apart from a few final adjustments/corrections that may assist to improve the manuscript.

**Level of interest:** An article of outstanding merit and interest 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'