Reviewer's report

Title: Test characteristics and potential impact of the urine LAM lateral flow assay in HIV-infected outpatients under investigation for TB and able to self-expectorate sputum for diagnostic testing

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Reviewer: Ruvandhi Nathavitharana

Reviewer's report:

Test characteristics and potential impact of the urine LAM lateral flow assay in HIV infected outpatients under investigation for TB and able to self-expectorate sputum for diagnostic testing.

This is an interesting, well-executed cross-sectional study designed to evaluate the role of urine LAM for TB diagnosis in the outpatient setting, which was nested within a randomized multi-center trial to evaluate the impact of Xpert MTB/RIF as a point-of-care test. Optimal diagnostic algorithms for TB remain elusive and currently need to be setting specific so the evaluation of a cheap, non-invasive POC test such as urine LAM in a primary care environment is of scientific and clinical importance. Other studies have suggested that using urine LAM with sputum microscopy or Xpert may add incremental benefit.

The study demonstrates that urine LAM testing had poor sensitivity in HIV-infected outpatients who are able to expectorate sputum as part of TB diagnostic testing and that there was no incremental benefit over Xpert or smear microscopy. They also evaluated potential impact on clinical outcomes by assessing indicators such as same-day treatment initiation but did not conclude that LAM could increase same-day treatment initiation except potentially in settings without access to chest radiography. The study was adequately powered to detect differences in diagnostic accuracy between LAM, Xpert and smear microscopy. Based on the study findings, urine LAM should not be used as an adjunctive diagnostic tool for HIV positive outpatients with symptoms/signs of TB who are able to expectorate sputum in a high burden setting.

Major Compulsory Revisions
- None

Minor Essential Revisions
- Were pregnant patients excluded?
- Why were patients who refused HIV testing combined as a group with HIV positive patients to constitute the group to undergo LAM testing? I'm not sure whether this is standard practice but I would consider adding rationale described in the figure legend to the text as well. The number of patients who refused is likely too small to merit sub-group analysis but could potentially cause false
results.
- Would suggest brief discussion regarding potential causes for false negative results.
- Would suggest brief discussion regarding how freezing might specifically affect results in terms of effect on sensitivity/specificity.
- page 5, line 12 spelling of diagnostics
- page 11, line 9, increase rather than increased
- page 17, line 10, spelling of Nocardia

Discretionary Revisions:
- It may be worth commenting on potential utility of LAM in children.
- Revise discussion so there is less repetition between paragraphs 2 and 5.
- Since TB treatment monitoring remains challenging, it may be worth discussing whether you think the potential prognostic utility for LAM in terms of risk of mortality merits further investigation.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

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

Declaration of competing interests:
I declare that I have no competing interests.