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: Paul Drain

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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”

Review for BMC Infectious Diseases
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The authors conducted a prospective study of various TB diagnostics, and conducted rapid LAM testing using frozen samples. Their conclusion is that urine LAM has limited diagnostic value where sputum Xpert and AFB smear microscopy is available, which may indeed be true.

My major concern relates to the conclusions that have been drawn. The Abstract Conclusion that ‘LAM offers no incremental value over Xpert or AFB smear’ is not entirely correct, according to their data. The authors reported a non-significant increase in diagnostic sensitivity when adding urine LAM to both tests, but this does not equate to “no incremental value”. The authors should also specify if they are referring to “diagnostic value”, since the value of a test also relates to accessibility and cost, where urine LAM is superior to AFB and Xpert. In this case, it would be most appropriate to change “value” to “diagnostic sensitivity”.

While urine LAM may not have had a significant increase for ‘same-day treatment initiation with CXR’, the number needed to test to identify one additional TB-infected person was only 12 people. For a 25-minute, urine-based, inexpensive test, that doesn’t seem so bad.

Their conclusions that urine LAM would ‘only improve Rx initiation in settings without chest radiography’ also does not seem entirely supported by their data. The data suggest that LAM may improve Rx initiation in settings without chest radiography, sputum microscopy, or Xpert.

The conclusion that “LAM is unlikely to impact TB-related morbidity and patient dropout” does not appear to be supported by the available/presented data. The authors should provide more justification or delete this phrase.

The authors report a significant association for urine LAM to predict patient outcomes, which should be mentioned in the Abstract Conclusion.
Using a higher grade of the urine LAM test (\(>=2^+\)) is likely to detect patients with a higher bacillary load, and may not be the most suitable threshold for a clinic-based test. At the clinic-based level using this threshold, one wouldn’t expect any increased sensitivity over Xpert or AFB smear, since they are also detecting a high bacillary-load infection. Using a lower grade (\(>=1^+\)) LAM as positive, the rapid test may have more clinical utility in an ambulatory setting. Therefore, the authors should also present results when using the \(>=1^+\) grade for the urine LAM test, even if as a supplementary table.

The study had 14 people did not have the reference gold-standard test ("contaminated culture or no available result"), this group should be eliminated from the analyses. The final cohort size should then be 569 people. Table 1 should then contain the description of this analyzed cohort (\(N=569\)), not the cohort of the parent study (\(N=1,095\)).

The authors’ statement that there is no available data on patient impact and mortality is not correct. They should cite/reference the following reference and cite the available published data about the (1) treatment response and (2) association with patient outcomes and mortality:


Since this is a longitudinal study, the authors should use Cox proportional hazards (rather than simple logistic regression) to assess the relationship to clinical endpoints (mortality/LTFU).

The study excluded those people unable to expectorate 2 sputum samples. The urine-based test may be best utilized in those who do not have a productive cough (i.e. able to expectorate sputum). Therefore, the authors should provide more discussion on how this exclusion may temper the potential impact of the rapid urine LAM test.

These analyses may have been better served to help guide primary-care clinics needing to introduce a rapid TB diagnostic test – should they implement AFB microscopy, urine LAM, or Xpert?

Minor Comments:
In the Abstract Results, authors state “583/1095 patients”, but the 1,095 is unnecessary. Just state, “Among 583 participants, ...”

The commentary in the Abstract Results, “would have had little impact on patient
“dropout” is interpretation of data and would be better served in the Conclusion section.

The authors state concerns about test sensitivity in the Abstract, but then do not comment on this in the Conclusions.

The grammar could be improved. For example, “Used at POC Xpert” is not proper English.

The authors should be clear that although 2 sputum specimens were collected, only 1 specimen underwent mycobacterial culture testing, which can result in diagnostic misclassification – leading to a lower specificity.

The authors show an association between urine LAM + and mortality/LTFU. Does this outcome differ when stratified by those started on anti-TB therapy and those not started on treatment?

The authors should also include citation of another LAM study in an outpatient setting:


This manuscript provides limited additional information from what has been previously published. However, as more data continued to be collected about urine LAM performance, these data will contribute to the conversation. I would recommend publication after major revisions.

**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, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests.