Reviewer's report

Title: Comparison of Xpert MTB/RIF with ProbeTec ET DTB and COBAS TaqMan MTB for direct detection of M. tuberculosis complex in respiratory specimens

Version: 1 Date: 11 March 2013

Reviewer: Andrew Christopher Whitelaw

Reviewer's report:

Summary:
The authors report on a comparison of the Xpert MTB/Rif assay, the ProbeTec assay, and the COBAS TaqMan assay, for direct detection of M. tuberculosis in sputum samples. They used a collection of stored sputum samples, all of which had been previously cultured. The overall sensitivity of Xpert in this study was similar to previous reports, although they did describe a slightly lower specificity than previously reported. The performance of the ProbeTec and Cobas assays was similar, with the ProbeTec being slightly more sensitive, while the Cobas had better specificity. However, none of these differences appear statistically significant.

The research was well conducted, and well presented, although I would recommend a review for language by a first language English speaker - the grammar is good, but in places can be simplified. I also feel that the paper would benefit from more statistical analysis and presentation of statistical data

Minor essential revisions:
Materials and methods; Specimen Processing and Culturing.
Please specify for how long cultures were maintained before being reported as negative; and please specify the rifampicin concentration used for susceptibility testing (or add an appropriate reference)

Results - when presenting the results of sensitivity and specificity please include 95% confidence intervals (probably easiest in a Table form). I would suggest revising Table 3 to show the overall sensitivity, as well as sensitivity for smear negative and smear positive patients; and then overall specificity (I do not think you need to break specificity down into culture neg and NTM, but this is discretionary).

Discretionary revisions / comments

Materials and methods; last paragraph.
I would suggest moving the last sentence of this paragraph ("Nevertheless, both assays... high capacity diagnostics") to the discussion section (and you may want to expand on this in the discussion). I think the ability of Xpert to be used on "low
tech" labs is a major advantage for the implementation of molecular testing in high incidence settings.

Discussion

Para 3: I don't think the conclusion that the sensitivity of 94.1% for smear pos samples is substantially lower than other studies' results is justifiable. If confidence intervals were available, it is likely that they would overlap with what was found in other studies. Suggest rephrase.

While freezing and thawing may have affected the yield of Xpert, it is also possible that the initial dilution and aliquotting of the stored sediment may also have affected sensitivity this limitations should be mentioned

Para 6: Rather calculate whether there was any statistically significant difference in the sensitivity and specificity of the tests, and then state that (rather than "differences were not immense")

Conclusion

The authors state that the improved specificity of the COBAS assay makes it more suitable for use in low prevalence settings. However, as the authors point out early on in the discussion, the calculated specificity of all the tests is influenced by the composition of the test panel - with I would suspect a disproportionately high number of NTMs (even for a low prevalence setting). I would suggest rewording it slightly to ensure this limitation is clearer.

Table 1:
I am not sure this Table adds substantially to the paper. If it is retained, I would try to simplify it. I do not think the "Scanty pos culture" column is of value - and the whole "culture" column can this be discarded. The table will thus show the breakdown of microscopy between the different groups of samples.

Table 2: I would remove this altogether - the information is in the text

Table 3: as suggested above, rather use this table to show the sensitivity and specificity, with 95% CIs.

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, and I have assessed the statistics in my report.

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