Reviewer’s report

Title: A commercial line probe assay for the rapid detection of rifampicin resistance in Mycobacterium tuberculosis: a systematic review and meta-analysis

Version: 1 Date: 10 May 2005

Reviewer: Tim Brewer

Reviewer’s report:

General

Overall it is a well done analysis.

Page 3, conclusions
As noted throughout the study, the operating characteristics of the LiPA are very good, and consistent across all of the studies examined. What additional evidence do the authors feel is needed “before LiPA can be used to detect MDR-TB...”? Based on these data, it would seem appropriate to consider using LiPA any place where MDR-TB rates are sufficiently high and resources allow. It would seem that cost-effectiveness analyses, rather than more data on LiPA testing performance, would help laboratories and public health organizations decide whether to include LiPA in their testing tuberculosis diagnostic strategies.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
None

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Page 2, Methods
I do not think there is a verb to "meta-analyze".

Page 3, paragraph 3
Though MDR-TB remains a major problem in many parts of the world, I did not think that the incidence of tuberculosis that multidrug-resistance was rising. Overall TB incidence is rising globally, but that may not be true for MDR-TB. The authors may want to confirm that the incidence of MDR-TB is rising, not just TB.

Page 6, paragraph 3 and figure 1
The manuscript should include some information about the 6 non-English, non-Spanish studies excluded from the analysis. Did these studies report similar test results to studies that were included? If not, how did their results differ from those studies that were included? If these studies were markedly different from the included studies, their exclusion may bias the results of the meta-analysis. If their results are very similar, then their exclusion is less likely to bias the results.

Page 11, paragraph 4
Without a cost-effectiveness or cost-benefit analysis it is hard to know whether the use of LiPA is "prohibitively expensive". Treatment for MDR-TB with second line agents is much more expensive than treatment for drug-sensitive TB. If an area has the resources to treatment MDR-TB, it may be
cost-effective to look for drug resistance even with LiPA at $116 per test (especially with selected testing based on epidemiologic criteria). If an area does not have the resources to treat MDR-TB, there is little point in looking for drug resistance even if the test was cheap. The issue of cost comes up again in the conclusion. The authors assume that because the test may cost $116, it is not practical for Eastern Europe, parts of India and China and elsewhere where MDR rates are high. This assumption ignores the costs of not rapidly diagnosing MDR-TB, which may outweigh those involved with testing.

Discretionary Revisions (which the author can choose to ignore)
Page 9, paragraph 5
When DNA probes for the diagnosis of TB were first studied, similar results were seen. Sensitivity was lower in clinical specimens, especially smear-negative one. There may not be enough data, but it would be interesting to know if test characteristics vary by sputum smear status.

Page 10, paragraph 4
To describe a scenario, using "For example" or some similar term may be more appropriate than "I will illustrate..." The reader does not know to which author the "I" refers to. This example, and the one that follows on page 11 assume that LiPA is used for all TB isolates. In low prevalence areas, a more useful (and clinically realistic) scenario would be to only use the LiPA when the index of suspicion for multiple drug-resistance is high. Because the pretest probability is higher, test retains its ability to discriminate between drug-sensitive and MDR-TB in a clinically meaningful way even in low prevalence settings.

Page 12, paragraph 3
It would be unusual, and very tragic, for a routine clinical setting to have an MDR-TB prevalence of 67%.

What next?: Accept after minor essential revisions
Level of interest: An article whose findings are important to those with closely related research interests
Quality of written English: Acceptable
Statistical review: No
Declaration of competing interests:
I declare that I have no competing interests