Reviewer's report

Title: Cost-effectiveness analysis of PCR for the rapid diagnosis of pulmonary tuberculosis

Version: 2 Date: 13 February 2009

Reviewer: Suzanne Marks

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1. Is the question well defined? Yes, cost-effectiveness of in-house PCR vs standard smear/culture

2. Are the methods appropriate and well-defined? Somewhat. There are some issues with language usage, so it is sometimes difficult to understand the current descriptions. However, several items should be better defined.

a. For example, there should be a clear description of the culture method used; I assume this is likely to be MGIT using liquid broth to enable a culture result in 2 days (the same as the period for in-house PCR results). Or, the paper is misleading in suggesting a 2 day result for culture, given that the time period and data appear to be similar to those used in the BMC published paper by the same authors in 2007 (BMC Public Helath. 2007; 7:356) in which the median time to MTB culture growth was 30 days and detection by PCR was 3 days. This would dramatically affect the cost calculations, as there would be patient work time lost waiting for culture result and a substantial difference between culture and PCR. And, both inpatient and outpatient costs would be affected. The current paper under review only finds cost differences for increased PCR lab costs, and not for patient costs and no difference between inpatient and outpatient costs.

b. The description of the cost analysis on lines 145-147 is unclear. Was the PCR dot blot not actually used, or why is the word “theoretical” inserted? It seems to me, based on the results section, that 2 strategies were compared: ZN/culture and ZN/PCR dot blot. Since culture is the gold standard, it might have been a better study to compare outcomes and costs of using the ZN alone for decision making compared with ZN/PCR, with sensitivity and specificities taken from each compared to culture or final clinical determination.

c. The use of the words “at least as cost-effective as ZN plus culture” is not sufficiently descriptive. When comparing 2 strategies, one strategy is either more or less cost-effective than its comparison strategy. If the authors are trying to say that the effectiveness is the same for both methods and that the costs did not differ significantly (and state the statistical method used to determine this), then that should be stated.

d. Were results stratified by HIV status? HIV was mentioned several times, but it was unclear what was done in the analysis.
e. You should reword lines 185-186. You are just stating that because culture is the gold standard and the PCR test results in some false positives, that treating those false positives is more expensive than if you had waited for the culture results and not treated them. But, usually, the decision to initiate treatment is based on the smear alone or some other clinical suspicion (as the culture usually takes several weeks to obtain), which also results in false positives that are treated. The real cost-effectiveness question is adding up the costs of treating false positives for each strategy and the costs of missing false negatives and comparing the costs of each strategy.

f. The discussion section mentions that mortality is an outcome that is important, but the current study did not even mention whether it was measured. With a high HIV prevalence, a missed TB diagnosis could rapidly result in death.

g. The discussion section mentions another strategy, ZN/PCR-AG, that was not presented in the methods or results.

h. Also in the discussion, a theoretical model for automated PCR is mentioned, but again, not mentioned in the methods or results.

i. Treating of returned false-negative patients is mentioned in the discussion, but again, not in the methods or results. Please explain what is a “returned false-negative patient.”

j. RX is not defined (chest radiograph?)

k. The cost effectiveness of rapid diagnostic methods versus standard smear and culture usually depend on the use and cost of respiratory isolation (rapid methods can quickly rule out infectious TB, usually longer time period to a negative culture result would result in longer treatment, hospitalization, and respiratory isolation), whether or not a contact investigation was initiated (which would not take place for MOTT), and whether a rapid TB diagnosis was not missed (which could result in transmission or death and lifetime productivity losses). However, by blinding the treating physicians to the results of the tests, decisions based on the results of the tests were not measured or modeled. While the current study design allows calculation of the sensitivity and specificity of each test, it does not allow a calculation of the actual costs and benefits of each test in a real world setting in which physicians are not blinded.

3. Are the data sound? I really don’t know
4. Does it adhere to relevant standards of reporting and data deposition? I guess so
5. Is the discussion supported by the data? See 2f-2h above.
6. Are limitations of the work clearly stated? I didn’t see a limitations section
7. Do the authors acknowledge any previous or ongoing work? They did not cite the 2007 BMC article that I mentioned in 2a above
8. Are the title and abstract accurate? Appears so
9. Is the writing acceptable? There are some problems with language that will need editing. On table 1, specificity of PCR dot blot is 85% not 84%. There are errors on Table 2, using commas instead of decimal points in the last column.

Major compulsory revisions: please address each item in number 2 above and cite the previously published work.