Reviewer’s report

Title: Sensitivity of direct versus concentrated sputum smear microscopy in HIV-infected patients suspected of having pulmonary tuberculosis

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Reviewer: Kristien Verdonck

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Many consider that concentrated sputum smear microscopy has a higher sensitivity for the diagnosis of pulmonary tuberculosis (TB) than direct smear microscopy, in HIV-seronegative as well as in HIV-infected individuals. The authors of this manuscript have found that this statement is not true in a population of hospitalized, HIV-infected patients in Kampala, Uganda. Their findings are in contrast with at least five published reports.

The manuscript is very well written, and remarkably transparent. The methods are appropriate to answer the central question. The results, figure and tables are very clear and convincing. The discussion is balanced and the conclusion is adequately supported by the data.

This study has potentially far-reaching implications. The recommendation to concentrate sputum samples in order to increase sensitivity appears to be based on insufficient evidence, at least for HIV-infected patients. In addition, it is possible that in this context in the past, studies with methodological flaws have led to overhasty and/or wrong conclusions.

A. Major compulsory revisions: none required.

B. Minor essential revisions:

B.1. The categories and numbers of excluded patients in the first paragraph of the results do not coincide with those in Figure 1.

B.2. Table 1. Data on mortality are missing for some participants. Does the “n=241” apply to the in-hospital mortality, the mortality at two months, or both? The last two p-values are not on the correct line. The abbreviation TB is mentioned in the legend but is not used in the table.

B.3. Table 2. The sub-title “culture-positive tuberculosis” is somewhat confusing because the calculation of the specificity is based on 109 participants with a negative culture. An alternative could be: “Diagnosis of tuberculosis based on culture”. The second sub-title could then be: “Diagnosis of tuberculosis based on culture or clinical criteria”.

B.4. Table 3. Non-Hodgkin’s lymphoma (NHL) is mentioned among the abbreviations but does not appear in the table.

C. Discretionary revisions:
C.1. The authors state that sputum concentration increases the sensitivity of smear microscopy for the diagnosis of TB in general, and find that this statement is not true in their study population of HIV-infected individuals. It would be interesting to know how the authors interpret this. Could HIV infection explain the differences in performance of the techniques? How? Or do the authors think that problems with study design might have led to wrong conclusions and recommendations, for HIV-infected as well as for HIV-seronegative subjects?

C.2. Was a sample size calculated before the study started? What were the assumptions (expected sensitivity, expected difference between the methods, expected number of exclusions)?

C.3. The proportion of positive culture results among TB suspects is very high in this study (61%), and the patients appear to have severe forms of TB with high mortality. How could this influence the findings? Could the advantage of the concentration technique in terms of sensitivity be higher among patients with mild or early forms of TB?

C.4. Results, p 7, third paragraph: “As seen in Table 2” could be replaced by “As shown in Table 2 (…)”.

C.5. The authors use the word “sex” in text and tables, except for the second paragraph of the results where “gender” is used.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests.