Reviewer's report

Title: Basis for treatment of tuberculosis among HIV-infected patients in Tanzania: the role of chest x-ray and sputum culture

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Reviewer: Stephen Lawn

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How to screen for active tuberculosis (TB) among HIV-infected patients in high TB-burden countries is an important one. Such data may have important implications not only for the detection of a key cause of morbidity and mortality in HIV+ patients, but also at a programmatic level in antiretroviral treatment (ART) programmes and isoniazid preventive therapy (IPT) programmes and also with regard to prevention of nosocomial TB transmission. This paper follows on from an earlier report on this study in which high rate of clinical and sub-clinical TB were found (Mtei et al CID 2003: 40; 1500-7). In this previous paper, the finding of a high rate of sub-clinical sputum culture positive TB was particularly important and this has also been found in a number of other more recent studies. It is becoming increasingly clear that symptoms are not an adequate screen to exclude active TB. Optimal means to screen for TB need to be investigated.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

Gold standard. The main problem I have with this study is that it presents a break-down of how 136 patients were diagnosed as having TB and were commenced on TB treatment. The relative merits of each of the ways of screening for TB are not compared to a gold standard or reference; reference is only made to the sum of patients who were ultimately treated for TB. This provides an audit of how TB diagnoses were established in this setting, but does not provide a scientifically valid evaluation of how to optimally screen for TB in this patient population. The validity of the diagnoses established by this cross-sectional study is not examined and as detailed below, there must be concerns regarding the evidence base for many of these.

Case definitions. No case definitions for TB diagnoses are given. Patients are simply categorised as ‘treated’ or ‘not treated’. Throughout the paper the outcome is only related to whether TB treatment was given or not rather than whether a case definition for TB was fulfilled. This is not a valid approach.

Positive microbiological diagnoses: These must be defined. Were just one or two positive samples required (smears or cultures)?

Patient assessment. A substantial limitation of this study is that patients were not
followed prospectively as part of the diagnostic process. Where diagnoses were not microbiologically substantiated, response to TB treatment or other clinical outcomes may have helped justify or refute these diagnoses. Some diagnoses were based on symptoms alone; the authors must provide justification for inclusion of these diagnoses. Again, case definitions must be included.

Sputum microbiology: Only 28% (38/136) of diagnoses had microbiological support despite obtaining sputum samples for mycobacterial culture in the majority. How were sputum samples obtained – was sputum induction used? To what extent was patient instruction given – this has a major impact on yield. Were 3 samples obtained from the 124 patients with results? What was the rate of loss of cultures in the laboratory due to contamination? The low rate of positive microbiology suggests possible over-diagnosis based on radiology / symptoms.

Radiology: Chest X-rays were read by a single radiologist who was not blinded to patient clinical assessment. Moreover the radiologist was undoubtedly aware of the previous finding of high rates of clinical and sub-clinical TB in this cohort. Thus, this cannot be regarded as scientifically rigorous. Radiology is a sensitive but non-specific investigation in this context. Over-diagnosis may have resulted in TB being diagnosed among 52 patients with no symptoms and negative (or absent) microbiology. Thus 38% of all TB diagnoses hinges on the opinion of a single non-blinded radiologist.

Mycobacterial blood cultures: All were negative. Although the authors remark that all patients were ambulatory and had CD4 >200 cells/µL, are there other potential reasons for lack of positive cultures? What technique was used? Were these processed locally or shipped to the USA as described in the previous paper? If so, were positive controls used to assess the effect of shipment on culture viability?

Extra-pulmonary TB: I can find no reference to diagnoses being made of extra-pulmonary TB (EPTB). In a cohort of HIV+ individuals this is unusual. Were patients assessed clinically eg for cervical lymphadenopathy? Were diagnoses of EPTB excluded? If not could they have been missed, thereby underestimating the true burden of TB?

Table 1. The denominators are inconsistent / confusing. Eg Did only 14 of the 136 TB patients have a TST done? If so why are they included? Why is history of previous TB only reported for 16 of the 136 TB patients? Etc etc.

Table 2. The denominators used in each of the cells are not clear and must be justified to allow interpretation. In the line with all TB diagnoses (n=136) the denominator used to calculate the proportion with a microbiological basis should be 136 and not 124 ie 28% of all TB diagnoses were microbiological. This Table is the absolutely critical part of the results section and it needs to be made much clearer.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of
Abstract. The abstract should include the overall proportion of patients whose TB was microbiologically proven.

Discussion, paragraph 2, reference 11. The CDC Botusa project has recently reported very contradictory findings to their Lancet report (see Samandari et al CROI 2007).

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

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.