Author's response to reviews

Title: Treatment outcome of tuberculosis patients at Gondar University Teaching Hospital, Northwest Ethiopia. A five - year retrospective study.

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Version: 2 Date: 18 August 2009

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The Editor

BMC Public Health

Re: MS: 2961839982776564- ‘Treatment outcome of tuberculosis patients in northwest Ethiopia. A five - Year retrospective study’

Dear Editor,

Thank you very much for your email of 28th July 2009. We are very grateful for the constructive comments forwarded by the reviewers. We have addressed their comments and have revised the manuscript in line with their suggestions. Below, we have provided a point-by-point response to the reviewers’ comments.

Sincerely,

Belay Tessema
Reviewer One: Bernt Lindtjorn

1. The authors review outcomes of tuberculosis treatment in Gondar in North-West Ethiopia. They analyse the records in a hospital's TB unit. Such studies are important, and provide important feedback for tuberculosis control.

2. The authors write: “However, treatment outcome of tuberculosis patients has not been assessed yet in northwest Ethiopia”. I suggest the authors do a literature search and add more references. Over the years, many studies were done in Gondar and in North West Ethiopia. Particularly, the studies by H Getahun, and M Demissie are important for tuberculosis control.

_We appreciate the reviewer’s comment and we have now done a literature search and added more references (Reference number 18, 23 and 32)._

3. The study is based on hospital data. The authors reviewed the TB registries. Did they also review the patient charts?

_No, we didn’t review the patient charts._

4. I advise the authors change the title. This is not a study about tuberculosis in North-West Ethiopia. It is a study about tuberculosis patients coming to a University Hospital.
We agree with the reviewer’s advice and we have modified the title as “Treatment outcome of tuberculosis patients at Gondar University Teaching Hospital, Northwest Ethiopia. A five-Year retrospective study”

5. I lack a thorough discussion of the limits in this study. Selection bias is present in such data, and the authors need to discuss this limit. I believe that by discussing the limits of the study, the authors will better communicate the challenges that institutions as Gondar face. Might be the authors should discuss how the tb work at a University unit should be integrated with the national control efforts?

We appreciate the reviewer’s comment and we have discussed the limits of the study in the discussion part (paragraph 7).

6. Only 16.8% of the patients were smear sputum positive. The proportion of smear positive cases in a tb control programme is often used as a quality measure of the control work. The smear positive rate in Gondar is a low, and makes me question the diagnostic setup at Gondar Hospital. How is the quality of their sputum examinations? Are sputum tests routinely done at the hospital? The large number of smear negative pulmonary tuberculosis is also an issue the authors need to discuss.

Yes, in Gondar University Teaching Hospital direct sputum smear microscopy for acid-fast bacilli (AFB) is done routinely following the national guideline for the diagnosis of pulmonary tuberculosis. Every individual suspected of having tuberculosis have an
examination of 3 sputum smears, to determine whether or not they have infectious tuberculosis. Three sputum specimens collected and examined in two consecutive days (spot-early morning-spot). However, this bacteriological method for the diagnosis of pulmonary tuberculosis has very low sensitivity ranging from 8.8% to 46.4% of culture-verified cases (Aber V R et al., Tubercle 1980). We also appreciate the reviewer’s point concerning to the large number of smear negative pulmonary tuberculosis and we have discussed this point in the discussion part (paragraph 6).

7. The authors include children in their study. Which criteria did they use to define tuberculosis in children? The authors should also refer to earlier studies on paediatric tuberculosis at their hospital. These paediatric patients are probable also included in the 4000 patients they report. See Ethiop Med J. 2007 Apr; 45(2):159-63

_Tuberculosis in children defined based on the criteria set by Federal Ministry of Health, Ethiopia, Tuberculosis, Leprosy and TB/HIV prevention and Control programme guideline using sputum smear microscopy, chest radiograph and histopathological examinations coupled with the history of contact with a smear-positive case and the presence of symptoms suggestive of TB._

Yes, some of the 212 children involved in the previous study might be included in 747 children involved in our study. However, in the previous study only hospitalized children (with special conditions) were involved. According to the Federal Ministry of Health guideline many children with TB can be managed on ambulatory basis and conditions that necessitate hospitalization include:
a) **TB meningitis or miliary TB, preferably for the first 2 months of anti-TB treatment;**

b) **Any child with respiratory distress;**

c) **Spinal TB;**

d) **Severe adverse events, such as hepatotoxicity**

8. The authors write that a patient with smear negative Pulmonary TB could be culture positive for *M. tuberculosis*? Is this a correct definition? If the hospital did not do cultures, the authors should use definitions appropriate to their setup.

*Corrected as per the reviewer’s suggestion.*

9. The authors write that they used the Ethiopian National TB Guidelines, “with some modifications”. They should tell the readers what these adjustments were.

*Some modifications were re-phrasing of the definitions to make short and clear rather than adjustments on the basic definitions of the treatment outcomes. We have now omitted the phrase “with some modifications” to avoid confusions of the readers.*

10. The authors did not mention HIV. Were patients not HIV tested? How many were on ART? In an important article in J Microbiol Immunol Infect. 2007; 40:116-122, Kassu A and colleagues report that over 50% of TB patients were co-infected with HIV in Gondar. This issue needs to be discussed.
Patient registration documents we reviewed lack information about the HIV status of our study subjects. However, a previous study conducted by Kassu et al showed that high proportions (52.1%) of TB patients were co-infected with HIV at Gondar University Hospital. We have now discussed this issue in the discussion part (paragraph 2 and 7).

11. Although the author’s conclusion is well-balanced, the discussion part of the article is weak. The authors should not repeat their results. They should discuss the limits of their work, how their findings compare with earlier research in North-West Ethiopia, in Ethiopia and globally. They should also answer the question on what the implications of this study are.

We are thankful for the reviewer’s constructive comment and we have avoided repetitions of our results on the discussion part, the limits of our work have discussed, our findings have compared with the findings of related studies conducted in Ethiopia as well as globally and we have answered the question on what the implications of this study are.

12. The authors should also look at the way they present their results. It might not be necessary to repeat the results in the text when they are presented in a table.

We have now tried to revise the result part of the manuscript.

13. On page 9 they write: “The number of smear positive pulmonary tuberculosis cases, smear negative pulmonary tuberculosis cases and extrapulmonary
tuberculosis cases did not significantly increase (p=0.48; CI: 0.47 -0.49). What does 0.47 -0.49 mean?

We appreciate the reviewer’s meticulous observation and we apologize for writing this sentence inadvertently, we have now omitted the sentence from the result part.

14. I advise that both the Crude OR and adjusted OR be presented in table 4. What did the authors adjust for?

We are grateful for the reviewer’s advice. Now both the Crude and Adjusted OR presented in table 4. All the variables in the table are included in the model to calculate adjusted OR.
Reviewer Two: Mark Cotton

Major compulsory Revisions:

1. HIV should be addressed as is a major co-factor.

*We are very thankful for the reviewer’s constructive comment. We have now addressed as HIV is a major co-factor in the introduction part (paragraph 2) and in the discussion part (paragraph 2).*

2. Where CI crosses "1", findings should be described as "trends", rather than definitive statements.

*We appreciate the reviewer’s comment and such findings have described as “trends”, rather than definitive statements.*

Minor essential Revisions:

For the diagnosis of TB, lack of culture facilities should already be integrated into the definitions of TB (page 6 and 7). For assessing treatment, does "negative bacteriology" mean "smear negative"? If so, this should be stated.

*Yes, it has now stated.*
**Discretionary:**

The site and region are mentioned 5 times (once in the introduction should be sufficient)

*We appreciate the reviewer’s comment and we have omitted unnecessary reappearance of the site and region of the study.*