Reviewer’s report

Title: Longer hospital stay is associated with higher rates of tuberculosis-related morbidity and mortality within 12 months after discharge in a referral hospital in Sub-Saharan Africa

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Reviewer: Suzanne Verver

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Review BMC infect dis Zetola et al hospital admission related TB incidence after discharge in Botswana

This elegant paper describes the risk of TB and TB related mortality one year after hospital admission and factors associated with it. It is one of the first papers on this subjects and uses creative and innovative ways to show the association. The paper highlights the relevance of TB infection control in hospitals and need for focus on ambulatory care. Discussion shows very important recommendations. It has a wealth of data and by trying to show all, some important details seem to be deleted.

Major Compulsory Revisions

1. In the objectives a 4th one should be added: to determine association between exposure during hospital stay and TB incidence and mortality during follow-up; since this is focus of analysis.
2. Methods para 2.1 and 4 use different definitions for TB. One seems to be for index cases, and one for cases diagnosed during follow-up. Why did author not use the same definitions?
3. In the analysis section calculation of persontime should be described. I assume persontime is from date of discharge till 12 months later, but cases are only counted for 9 out of 12 months. I wonder whether persontime should be reduced to 9 months. If not, reason should be made crystal clear.
4. It seems some associations are given in results text while detailed numbers are missing. Maybe due to lack of space some tables were omitted; but they are necessary to convince readers.
   a. Before multivariate, also univariate odds ratios should be given; probably in an adapted table 3. Table 3 should also have a line of totals. The methods and results refer to association for mortality; but associations for mortality are not given.
   b. There should be more clear division between dependent and independent variables. It seems that in table 3 dependent and independent variables are different from table 4 and 5. For example in table 3 exposure index seems dependent, while in table 4 and 5 it is dependent. When this is on purpose please give reason.
c. Methods para 5: statistics: Fisher’s exact or Wilcoxon-rank-sum test: results are not given. Use of ART is evaluated as confounder, but results are not given (except description). Smear positive 1+, 2+, 3+ and chest x-ray results are evaluated as severity of disease but no association results given. Maybe for all of these OR changed less than 10%, but that should be indicated in results.

d. Results last para, last sentence: ‘particularly resistant TB’: these results are not given.

e. Why is days spent in cohorting bay not in table 4 and 5? It is described in abstract that this measure is compared to total hospitalization and ‘number and proximity to TB index case’ and that ‘performance’ is similar. In discussion it states: ‘similar level of associations’. From table 3 it seems cohorting bay was probably not significant (although no OR given); while total hospitalization and ‘number and proximity’ were significant. So the performance was actually different. Can you clarify? Rather than performance or association, better to specify as adjusted odds ratios (if that is what you mean).

f. Discussion states: ‘without reaching a plateau’. Curves are not shown. Can they be put in online supplement? Or delete this sentence.

5. Table 3: how can the TB related mortality be higher than the overall mortality in the rows for CD4 count and diagnosis of PTB during admission?

6. Table 5: column 3: strange that an OR of 1.0 has p of <0.01? I assume this OR means increased odds for each day extra? Maybe useful to explain in methods or results and add decimals where appropriate.

Minor Essential Revisions

1. The annual rate of TB cases during follow-up mentioned in the abstract (3712/100,000) should be repeated in main text. Since number of personyears is much less than 100,000; this gives false idea of precision. Maybe better to use 4/100 pyrs. Further it does not seem to agree with table 3? In table 3 probably ‘per 100,000 pyrs’ should be ‘per 100 pyrs’?

2. Abstract states: number and proximity to index case. These seem 2 different measures. You mean ‘composite measure of exposure combining number and proximity to index case’.

3. Background last paragraph, first sentence: ‘have been extensively studied’. This needs a reference for TB.


5. Methods paragraph 2: which environmental factors were collected and how have they been used in analysis? Maybe not used, so can be deleted?

6. Methods para 2.1 versus 2.2: in 2.1 cultures are not mentioned while they are given in 2.2. Does hospital not have culture results but clinic may have them? Or they usually become available after discharge? Or maybe this is just an omission in para 2.1? Similar does para 2.3 refer to smears and cultures?

7. Para 2.4: what happened if x-ray readers disagreed on severity?
8. Para 3: what is the difference between those lost to follow-up (=untraceable?) and those not seen but assumed to be alive? In the results it seems 8.6% was lost to follow-up (which is fantastic that they are so few in such complicated study); but there are many more who are assumed alive and have no TB.

9. Results last para, last sentence: history of prior TB infection. Do you mean ‘TB disease during admission’?

10. Table 1: Some categories do not add up to 1094. Rest is unknown? Please indicate so, or correct. Check other numbers.

11. Table 4 and 5: add n for each column. Add a line between variables ‘total days admitted’ and ‘days of adjacent exposure’.

12. Figure 2 is very difficult to read; can this please be redone? Some of my questions may be answered when this figure is better readable.

Discretionary Revisions

1. The authors collected an enormous amount of data and maybe the paper should be split in 2 papers; one on factors during hospital stay (focusing on objective 1), and one on the follow-up period (which is the main focus on this paper). Alternative; objective 1 in itself can be deleted, since this is just information collected to analyse the association between exposure and TB incidence (that I referred to as objective 4 above). This may also reduce the description of a lot of data collected that were actually not used in analysis (see above).

2. In order to shorten these parts may be deleted:
   a. Para on Xpert in introduction (since this is repeated in discussion)
   b. Methods para 4: Sentence on tuberculin (this is isolated statement)
   c. Details of diagnosed cases in methods para 4 (since not used in analysis)
   d. Table 2 not relevant for message of the paper.

3. Para 5: ‘Finally….’. This can be labeled as sensitivity analysis?

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests