Reviewer's report

Title: Factors influencing specialist care referral of multidrug- and extensively drug-resistant tuberculosis patients in Gauteng/South Africa: a descriptive questionnaire-based study

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Reviewer: Hendrik Simon Schaaf

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The study is of interest as reasons should be determined why patients diagnosed with drug-resistant TB do not get appropriate treatment. This may differ in different settings. However, this study is not quite clear on methods or results and can benefit by improving these sections. The reviewer has the following comments:

Major comments

1. Abstract:
   - The last two sentences of the conclusions cannot be made from the study results, as this was not studied, but is only presumed

2. Background:
   - page 5: the aim(s) of the study is not clear: to determine the number of culture and DST confirmed MDR/XDR-TB cases not on treatment and to determine the reasons why treatment was not started? The rest does not belong to the aims of the study. Last sentence definitely should be deleted.

3. Methods:
   - The methods are very confusing – especially study design and data collection! What was the entry point to the study? Were patients primarily identified from the NTBRL database? How were they linked to the 40 healthcare facilities? Adults are >18 years of age, so if children/adolescents 13-18 years are included it should be stated as such (they are not adults). The definition of an MDR-TB case is most likely also not correct, as if one reads it as is stated here, only those patients “not on treatment” were included – cause for bias, but what treatment is referred to – no TB treatment, no second-line treatment, no previous TB treatment?
   - A second problem in the methods is as follows: the study was conducted Oct-Dec 2008, and culture/DST results were collected for the period Jan-Jun 2008 – why did the investigators look for these patients in Sizwe Hospital’s records between Jan-Jun 2008? As far as the reviewer recollects from that time, rapid diagnosis of MDR/XDR-TB was not yet freely available, and even if
diagnosed/confirmed as MDR/XDR-TB, it would have taken any clinic some time
to trace the patient and arrange for referral/admission – should there not have
been a lag period of at least a month or two be provided for – therefore looking
for admissions until end of August 2008? Also, in this part of the methods it says
that data was collected on “previous treatment for TB” – which was not part of the
case definition. Should the data not have been collected at the NTBRL, traced to
health care facility who sent the specimen and then from there see what
happened to the patient (admission to Sizwe, not traced, etc)? Thereafter one
could look through Sizwe’s register to see who was actually admitted?

- The third question – what was the questionnaire about? Was this about specific
patients or a general questionnaire on how newly diagnosed patients (or new
MDR/XDR-TB results) are/should be managed at that facility?

- Statistical analysis: responses are from staff, not health care facilities?

- What are the definitions used for “loss to follow-up, not traceable/contactable,
did not come for results” (table 2)? These seem very similar if not the same to the
reviewer? Definitions should be part of methods

4. Results:

- page 7, 2nd paragraph: It is not clear at all from the methods how this data on
what happened to the patients/results were collected – was this part of the
“semi-structured questionnaires”? Was there a questionnaire for each facility or
for each patient identified at the laboratory? 118 cases “were not informed about
their positive culture results” – was this obtained from the health care facility or
from patient/family member (as many of them died)? If they were already
deceased when traced, they could not have been referred – surely this refers to
tracing of patients to recall them for referral? The reviewer thinks that both the
methods and results sections need careful reconsideration and rewriting.

5. Discussion – this should receive attention in view of the all of the above!
Patients should be diagnosed, then traced and only then referred? Although it
probably true that much of this is easily rectifiable, someone should still take
responsibility – a word not mentioned but essential!

6. Conclusions: has little to do with the current study

7. Table 1: the heading should reflect the fact that this represents data only from
40 clinics/hospitals and from 4/6 districts

8. Table 3 – this does not really give clear reasons why patients were not traced
and referred – not sure how this data fits in, and if it does, should be discussed in
the context of the study (discussion).

Minor comments:

1. Abstract:

- line 6: authors use “non-transferral” in this context, but in the text following this
as well as in main manuscript use “non-referral” – it is important to be clear on
what they mean (definition) and to use same terminology throughout

- lines8-9: drug-susceptible TB rather than drug-sensitive, as it is also drug
susceptibility test(ing)
- line 11: $97 + 2 = 99\%$? Should be 100%
- line 12: “loss” not lost
- line 13: Delete “Nearly”

2. Background:
- line 3-6: WHO data of 2011 are already available, why use old data of 2008?
- line 4: Write out words in full before using abbreviations in body of the manuscript (e.g. MDR-TB, XDR-TB)
- lines 10-12: The whole sentence from “WHO …” to “…2011-2015.” Should be deleted as it has no relevance to this study at all
- line 16: health care providers (I wish we could provide health!)
- line 18: the reviewer is not sure what is meant by “developing persistent disease” other than progressive destruction (or disease)? Should death not be added to the list of consequences of delays in diagnosis?
- lines 20-21: the authors are, in this sentence, most likely referring to their own setting or to high-burden, low resource TB settings, as they also refer to “excessively” (should be deleted – unnecessary word) high HIV co-infection rates. This is not clear from the description as the general background just flows into their own/high burden setting? Also, not only early detection but also early treatment of drug-resistant TB is important (same goes for end of 2nd paragraph of page 4)
- page 4, 3rd paragraph, lines 5-6: Sentence should be rewritten – repetition in sentence
- page 4, 3rd paragraph, lines 9-13: Suggest rewriting as follows: “…and referral of drug-resistant cases. If patients are diagnosed with MDR- or XDR-TB, they are referred to Sizwe …(SH) for treatment, a 268-bed specialized treatment centre for MDR- and XDR-TB patients.”

3. Results:
- page 7, line 3 – percentages should add to 100%
- the inclusion criteria specified age >13 years, but range is from 10 years and up?

In all, the reviewer thinks that the data holds promise, but that the presentation of the methods and the results (and then discussion) still needs some reconsideration/replanning and rewriting.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published
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'