Author's response to reviews

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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Author's response to reviews: see over
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

Version: 1 Date: 4 February 2013

Reviewer: Hendrik Simon Schaaf

Reviewer's report:


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
   We acknowledge that the second-last sentence can be considered as controversial if presented as conclusion from this study and consequently, this sentence has been removed. However, we are confident that it can be concluded that TB focal points need strengthening, and would wish to retain this last sentence.

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.
   This has been re-phrased and the last sentence has been deleted.

3. Methods:
   - The methods are very confusing – especially study design and data collection!
   We have sought to provide more clarity. We try to address all questions raised in the revised Methods section and respond to them as far as this would not lead to repetition, or as far as we cannot see that initially made statements could be clarified any further. What was the entry point to the study?
   This is clearly and concisely described in the Study Design Methods sub-section.

   Were patients primarily identified from the NTBRL database?
   This is now clearly and concisely described in the Study Design Methods sub-section.

   How were they linked to the 40 healthcare facilities?
   This is now clearly and concisely described in the Study Design Methods sub-section.

   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).
In fact, we looked at all referrals (as applied for and approved of in the study protocol) which were diagnosed with DR-TB. We have corrected this and removed the misleading ‘adult’ from the patient cohort description from the beginning of the Study design Methods subsection.

**The definition of an MDR-TB case is most likely also not correct,**

We do not understand this remark and reject it as not acceptable.

**As if one reads it as is stated here, only those patients “not on treatment” were included –**

This actually indeed requires clarification as unexpectedly for us as we still think that this was clear from the paper’s context – should have stated: ‘not on treatment for DR-TB’ – this has been rectified in the revised version.

**Cause for bias, but what treatment is referred to – no TB treatment, no second-line treatment, no previous TB treatment?**

We understood it was only logical and evident from the literature that the patients diagnosed with DR-TB would be a mix of patients with initially DS-TB which became DR-TB over time due to the usual range of possible reasons; as well that there is an increasing number of patients with primarily DR-TB diagnosed following an initial drug sensitivity assessment of the first isolate before DR became evident from non-responsiveness to treatment. In the face of space constraints and partial self-evidence of this, we are keeping this section concise, but we trust this is now clearer also for readers not familiar with DR-TB patient care.

- 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?

We have tried to provide further clarification whilst not blowing up the method section beyond what is feasible within the usual space constraints.

The answers to the main questions raised above are (now) evident from the methods section, and it is phrased as it should be according to the reviewer’s understanding and suggestions.

The NRTBL conducts the resistance testing (full assessments; specimens received were tested for the full panel of drugs; some of the specimens may have been sent on the basis of rapid testing – not freely available at that time but that has nothing to do with what we are addressing here; others on clinical grounds of suspected DR-TB either in patients not, or patients treated before for TB) on specimens sent from the various health care facilities; then feeds back the results to them, and then ideally those facilities begin the tracing/referral procedure. We started looking into this whole question because we noticed that there was a mismatch between the number of patients being referred to us and the number of diagnoses made in the NRTBL and being reported back to the diagnosis-requesting health facility. Now, we conducted our study in the second half of 2008, looking into the referral of patients whose DR-TB was diagnosed and reported back from NRTBL to the health facility between January to June that year. As their seemed to be no significant delay between obtaining DS-testing results at the NRTBL and feeding back the results to the test-requesting health facility, we focused on looking at the time lapse between arrival of
the test results at the facility to referral point-in-time. To that end, the methodology to look into the time period from January to June without a gap month appears just to us. More so even in view of what we discuss in the first paragraph of our discussion, namely that timely referral is paramount for minimizing loss of lives.

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?

We are not sure we understand the question. The notion that we collected data on previous treatment for TB indicates that we asked whether a patient received treatment for (DS) TB before; as those data, in the end, did not have any direct consequence for the referral process, we did not report results on this.

Regarding the procedure; we cannot really see what the reviewer’s suggestion for the methodological plan is, i.e. in what way it would differ from what we did:

1) The study was initiated by the SH physicians who were confronted with ‘two realities’: the NTBRL data indicating which patients were diagnosed in a given period of time with DR-TB; and on the other hand the patients being referred to Sizwe Hospital.

2) Realizing this mismatch we embarked on analyzing this situation.

3) We therefore took the NRTBL data, and matched those with the patients having been referred from the different health facilities.

We understand we made that clear in the methods but have looked at every single word again to make sure this is understandable.

- 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?

This was elaborated on already in the Methods section before, but we tried to restructure and make it clearer for better understanding. The downside is that the text is becoming clumsier and longer; however, if this clarifies things we understand this will be acceptable.

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

As said in the Methods section: Health care professionals at these institutions were interviewed using semi-structured questionnaires. However, we tried to further clarify this.

- 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

We tried to tell those with a first contact after obtaining the diagnosis and those who were directly lost apart, but we agree this is somehow constructed and not helpful; we merged those two rows; all else is self-explanatory and does not be elaborated on any further in the Methods section.

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”?

This should be clear by now from the Methods section.

Was there a questionnaire for each facility or for each patient identified at the laboratory?
As elaborated on in the Methods: Part A of the questionnaire was on the Health Facility’s (HF) referral practice; part B was on patients seen at this HF diagnosed with DR-TB at the NRTBL but later not referred from this HF to SH. No questionnaire was done for those patients successfully identified and referred to SH (we understand this is self-explanatory).

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.

We have clarified those issues in the revised version’s results section.

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!

After having been diagnosed at the NRTBL, and after the results have been sent back to the diagnosis-initiating health care facility, it is of course then the task for the diagnosing-initiating facility to trace and refer the patient (which is what this paper is about). This also clarifies responsibilities. We have, however, tried to make that clearer in the discussion.

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

The conclusions section has been rephrased now.

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

Done.

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).

We respectfully disagree and think it does. The reference to table 3 has been extended.

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
   Done.
   - lines8-9: drug-susceptible TB rather than drug-sensitive, as it is also drug susceptibility test(ing)
   Done.
   - line 11: 97 + 2 = 99%? Should be 100%
     We thank the reviewer for this correction; it should be 97% and 3%.
   - line 12: “loss” not lost
     Done.
   - line 13: Delete “Nearly”
     Done.

2. Background:
   - line 3-6: WHO data of 2011 are already available, why use old data of 2008?
     We have chosen to use the numbers from 2008 as the data described in this study are from the same year.
- line 4: Write out words in full before using abbreviations in body of the manuscript (e.g. MDR-TB, XDR-TB)
Done.
- lines 10-12: The whole sentence from “WHO ...” to “…2011-2015.” Should be deleted as it has no relevance to this study at all
Done.
- line 16: health care providers (I wish we could provide health!)
This has been changed to health care facility.
- 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?
‘Increased mortality’ has been added.
- 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)
This has been clarified and the necessity of treatment has been added.
- page 4, 3rd paragraph, lines 5-6: Sentence should be rewritten – repetition in Sentence
Here we address the situation in South Africa, the previous paragraph describes more the global situation.
- 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.”
Done.
Done.

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

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'