Reviewer's report

**Title:** High levels of Multidrug Resistant Tuberculosis in new and treatment-failure patients from the Revised National Tuberculosis Control Programme in an Urban metropolis (Mumbai) in Western India.

**Version:** 1  **Date:** 23 March 2009

**Reviewer:** Dag Gundersen Storla

**Reviewer's report:**

Major impression

The study is conducted in Mumbai, one of India’s megacities, with a large part of its population living in densely populated slum areas, with an expected high transmission of tuberculosis. It has long been anticipated that the proportion of MDRTB in India has been low in not previously treated cases. This study is an important wake-up, that there is an alarmingly high proportion of MDRTB, not only in tertiary institutions but also at health posts; 24% in not previously treated cases and 41% in treatment failure cases. It appears to be a well conducted study, with convincing results, which have been verified both by thoroughly conducted internal validation and an international reference laboratory. My overall recommendation is that this article should be published by the BMC Public Health.

Before it can be published, however, substantial revisions are needed. Important information needs to be added and extensive work on language and syntax needs to be done. The language is old-fashioned and intricate, sometimes the sentences are extremely long, and you have to read them several times to understand what the authors actually are trying to say. The language should be simplified, with less use of passive tense and with shorter sentences.

**ABSTRACT**

1. Generally avoid abbreviations, especially if they are not spelled out: DST, RNTCP, H, R, etc.

2. Abstract: Do not introduce issues that are not explained. Remember that most readers only read the abstract. What is “category 1”? For those of us who know the term well (including me) it is obvious, but not to all readers.


4. Abstract: Conclusions: “are at considerable variance from projected national estimates” – Why this unclear way of expressing it? You have found a dramatic increase in MDR compared to former estimates. You should dare to be bolder. Also about the consequences of your findings.

**INTRODUCTION**

5. Introduction – page 5 – line 1: If you mention the “80%” - you should mention
how many countries this comprises – preferable list them. But this is not needed
in this context. It is better to omit it, mention that India is considered a hot spot for
MDR and keep the information that India, China and Russia accounts for 62% of
the world’s MDRTB.

6. Page 5 – line 8: Perhaps comma after “Additionally”?

7. Page 5 – line 12: Sentence too long. It should be a break after “MDRTB
cases”.

8. Page 5 – line 14: Comma after “110,132”

revising the whole sentence; it is too long and not easily understandable.

10. Page 6 – line 4: Too long sentence; stop after “re-treatment cases” is
needed.

11. Page 6: The findings from the “tertiary clinic” need to be more thoroughly
discussed and the sentence revised.

12. The term XDR-TB is introduced, but not explained. Why use XDR-TB and not
XDRTB (you are all the time using MDRTB – you have to be consequent.

13. Page 6: There are other studies from Mumbai tertiary care institutions that
need to be mentioned, for example Rodríguez et al., who find an even higher
number of 68% MDRTB among all isolates (percentage of new and previously

14. Page 7: Last sentence should be deleted; that you have ensured good quality
research is actually what you are going to justify in the coming Materials and
Methods chapter.

MATERIALS AND METHODS

15. Page 8: Do not mention the wards by abbreviations, spell them out. It is not
mentioned why these wards were selected, and if randomly selected; how the
randomization was done. Why slum areas – not a mixture of slum and middle
class areas?

16. Page 8 – sample size: again, you do not explain “Category 1” to the reader.

17. Page 8: “Figure 1” should not appear in the headline, or at least be included
in the sentence before the colon.

18. Page 8 – third line from the bottom should be changed: “sputum-smear
positive” not sputum smear positive.

19. Page 8 – line 10: You should explain DOTS; spell it out and briefly tell what it
is.


21. In the passage on recruitment nothing is mentioned about how the patients
were selected. Under results you state that 1453 were screened. Were these all
cases of this specific period, the first 10 patients every day, etc.? If randomized,
how was the randomisation done?

22. Drug susceptibility testing (page 10-11): How many originally included were
excluded because of contamination or other reasons? How did you verify that a strain was member of the MTB complex?


24. Page 11 – 6th line from bottom: Epi Info not Epiinfo

25. Page 11 – third line from bottom: “Stockholm” is not needed, or should alternatively have commas on both sides.

RESULTS AN DISCUSSION

26. Page 15: The above mentioned study by Rodrigues et al. published in 2006 finds 68% MDRTB – higher than the range 11-48% of the study you refer to – this should be included in your discussion. Unfortunately, no previous studies give exact numbers for new versus previously treated cases. Your study is the first to do so, this is an important point.

27. The term “new” patients is problematic. You cannot principally know if they are primary, reactivation, etc. It is better to use “not previously treated”.

28. You should discuss the main factors driving the development of MDR on the Indian sub-continent; That most patients are treated by private practitioners, that there are no restrictions on the sale of TB drugs to everyone everywhere, the vicious circle of repeated visits at the same level without reference to the NTP, the lack of drug testing facilities; why it is so difficult to establish and keep running with a good quality level, the mismanagement and low motivation among the workers in parts of the government NTP, etc. These are important issues that are not readily addressed and discussed in your paper.

29. A major point: A majority of your cases are probably due to reactivation (the fingerprinting study), the transmission took place maybe decades ago when I and S was used in monotherapy. If I resistance exist, MDR will often follow. You should discuss how the history of drug policies has influenced your current situation along with taking into account the current influence of Beijing strains (35%).

30. The fingerprinting study is not yet published, but you should consider at least referring to these issues, and find out how you could overlap in a fruitful way without prepublishing data of the other study.

31. Page 15 – bottom line: you should write R and not rifampicin, since this abbreviation has already been introduced.

32. Page 16 – first line: You have not explained to the reader why the presence of a mutation in the rpoB gene is sufficient as a marker for R resistance. (It is not spelled with beta). There should also be a comma between “assay” and “which”.

33. You quote several studies – a dot should be after “et al.”, which you systematically omit.

34. Page 16 – line 15: Did you selected so that not previous MDR cases in your treatment failure group were included? How is this possible if DST was not performed last time the patient was treated? Or do you refer to the not previously treated cases when you speak of stringent screening? This whole passage is
unclear and must be revised.

35. Page 17 – line 10: you should write more than 3, not >3.
36. Page 17 – line 13: [1] in the end of the sentence. The implications of increasing XDR are not properly discussed; especially in a low resource setting this is a possible catastrophe.
37. Page 18: Previously you have used i) and ii), here you are using a) and b) – you should make a consequent choice.

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

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

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.