Author's response to reviews

Title: Factors associated with the low cure rate of tuberculosis in the remote poor areas of ShaanXi Province, China: a case control study

Authors:

Xianqin Ai (axqfzhk@126.com)
Ke Men (menke@foxmail.com)
Liuji Guo (sxiec@163.com)
Tianhua Zhang (zthfzhk@126.com)
Yan Zhao (zyfzhk@126.com)
Xiaolu Sun (sxlfzhk@126.com)
Hongwei Zhang (zhhwfzhk@126.com)
Guangxue He (heguangxue@chinatb.org)
Marieke J van der Werf (vanderwerfm@kncvtbc.nl)
Susan van den Hof (vandenhofs@kncvtbc.nl)

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Author's response to reviews: see over
Dear Miss Colette Homan,

Thank you very much for your email of 27 January 2010, with regard to my revised manuscript (Ms. Ref. No.: 1857418540305996) together with the comments from the reviewers. We carefully read the comments and suggestions and have now completed a revision of the manuscript that addresses their concerns.

As you will see in the revised manuscript, we have revised parts in the original manuscript according to the reviewers’ comments. We also responded point by point to each reviewer comment as listed below, along with a clear indication of the location of the revision. Revisions have been made throughout the manuscript to improve English language and were checked by a native English speaking colleague. In the background section of the abstract we included contextual information.

We thank the reviewers for their constructive suggestions that have improved both the quality and the clarity of the manuscript and we hope that the revised manuscript is acceptable for publication.

Thank you very much for your continued attention.

Yours Sincerely,

Ke Men
Ph.D., Associated Professor,
Department of Epidemiology
The Fourth Military Medical University
17 Changle Western Road
Xi'an, Shaanxi, 710032
P. R. China
Email: menke@foxmail.com
Fax: 86-029-84774868
We acknowledge both reviewers’ comments and suggestions very much, which were valuable in improving the quality of our manuscript. Please find below our point-to-point response to the reviewers’ comments:

Replies to Reviewer Dr. M A Hamid Salim:

Comment:
5% patients stopped treatment due to auditory impairments. Since the regimen does not have Streptomycin. I do not see which drug can cause it? How these auditory impairments have been assessed?
Reply: According to design of the study, patients were interviewed by the investigators with a standard questionnaire. The recording of adverse effects including auditory impairment was based on self-report of patients. Although the standard regimen for all patients from designated CDC TB clinics does not contain streptomycin, our investigation showed that some patients did get additional drugs from other clinics while at the same time being treated by CDC TB clinics and it is possible that it is added to the regimen in some patients.

Comment (continued):
In the text it was expressed that "39.3% did not have medical insurance which means that they needed to pay for all medical costs themselves except for the anti-TB drugs which are provided free of charge." The people those who have no insurance what kind of medical costs they are suppose to pay during TB treatment?
Reply: Medical costs of TB treatment include costs for hospitalization, tests other than smear-examination, and other drugs except for the free standard regimen. The people who have no insurance are supposed to pay for them. We have added this to the text.

Comment (continued):
Other comment: text needs still some revisions. The word re-examination, written in several places as reexamination.
Reply: As the reviewer suggested, we revised the manuscript.

Replies to Reviewer Dr. Peng Wu
Comment:
1. For the additionally included non-cured patients, I still don’t think it is a proper way to deal with the observed increased non-cure rate in terms of the study objective and study design. I therefore suggest that the authors redo the analyses after excluding the non-cured patients added to the original sample after observing an increased cure rate in the study population compared to 2005, to see if the authors could get wider confidence intervals for the parameters estimated in the model, or the final results of the analysis would
change. Besides, the authors should mention the comparison of the results of the two analyses in the limitations of the study if there is no change between the new analysis and the old one.

Reply: The sample size calculation of the study was based on treatment outcome information of TB patients in 2005. Uncured and cured patients diagnosed between June 1, 2006 to March 31, 2007 were randomly selected from 30 counties. During the study period, we observed an increased patient cure rate in the study population compared to 2005. So the number of uncured patients was small and we decided to include all uncured patients registered. This change did not break the design principle of case-control study and thus was not expected to affect results, except increase power and thus reduce the width of the confidence intervals.

We redid the analysis after exclusion of the 45 non-cured cases later and the results were very similar. Due to a loss of power, in univariate analysis the OR was not significant any more for fever, loss of appetite and maximum number of subsequently missed doses but trends in OR’s were very similar. Major risk factors were still included in the multivariate model excluding the additionally added 45 cases with similar ORs: both models included comorbidity, interruption of treatment, DOT supervisor, institute where TB was diagnosed, and regularity of sputum re-examinations. We have mentioned that results were similar in the limitations section of the discussion.

Comment (continued):
There might be some errors in table 3 and 4 in terms of the alignment and/or the values of P-value, especially the P-values in the table 4. Please check them again carefully.

Reply: As the reviewer suggested, we checked table 3 and 4 again carefully in the manuscript. There were no errors in the tables. We deleted p-values from Table 4 as they are redundant for the multivariate model.

Comment (continued):
3. Based on the reply to the third comment in the first review, “There was no significant difference between non-cure (rates) for those with a doctor or family member as treatment observer, as the confidence intervals overlap” is not a correct way to interpret the results of the statistical analysis and justify the conclusion the author drew in the paper.

Reply: We calculated the relationship of family member and doctor as DOT supervisor.

Table. The relationship of family member and doctor as DOT supervisor

<table>
<thead>
<tr>
<th>DOT supervisor</th>
<th>n ( % )</th>
<th>Uncured (%)</th>
<th>Cured (%)</th>
<th>OR</th>
<th>95%CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family</td>
<td>367 (78.1)</td>
<td>73 (19.9)</td>
<td>294 (80.1)</td>
<td>0.06</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Doctor</td>
<td>103 (21.9)</td>
<td>12 (11.7)</td>
<td>91 (88.3)</td>
<td>1.88</td>
<td>0.98-3.62</td>
<td></td>
</tr>
</tbody>
</table>
Indeed, the non-cure rate seemed better for those with a doctor as treatment observer than for those with a family member although there was no significant difference between them \((P=0.06)\). This may be due to small sample size of patients with a doctor as DOT supervisor. We have adjusted the text to clarify and soften the conclusion.