Author's response to reviews

Title: Tuberculosis recurrence and mortality rates in successfully treated tuberculosis patients in southern Ethiopia: retrospective cohort study

Authors:

Daniel G Datiko (danieljohn42@yahoo.com)
Bernt Lindtjørn (bernt.lindtjørn@cih.uib.no)

Version: 3 Date: 20 April 2009

Author's response to reviews: see over
Reviewer #1

Reviewer Name: Kalappan Pillai

The reviewer’s comment: Major Compulsory Revision

1. Recurrence rate can be restricted to smear positive patients only. Smear-negative and EPTB may be excluded from the analysis of recurrence of TB as the diagnosis of recurrence is ambiguous.

I respond to the reviewer’s comment as follows:

We agree that the uncertainty of diagnosis is greater in smear-negative and extrapulmonary TB patients. The diagnosis of smear-negative and extrapulmonary TB was conducted according to the recommendation of the National TB and Leprosy Control Programme as described under methods in the section of case definition, treatment duration and outcome. However, we have added to address this limitation.

The revised part of the discussion on page12 paragraph 2 line 3 now reads:

Using clinical examination, sputum examination and x-rays for the diagnosis of recurrence in smear-negative and extrapulmonary TB cases may have contributed to the over diagnosis of the cases.

The reviewer’s comment: Major Compulsory Revision

2. Recurrence can be reported separately for cured cases and completed cases.

I respond to the reviewer’s comment as follows:

Of the 425 smear-positive patients, 399 (96.2%) were reported cured and 26 (3.8%) treatment completed. There were 15 cases of relapse among patients who were cured but
none in those who had completed treatment. There was no difference in the rate of relapse in the two groups (log rank, p-value = 0.18). We have added a sentence to results section.

*The revised part of the results section on page 9 paragraph 2 line 6 now reads:*  
In smear positive cases, there was no difference in the rate of relapse between patients reported cured (3.75 per 100PYO, 15/400 PYO) and treatment completed (0 per 100PYO, 0/26 PYO) (log rank, p-value = 0.18).

**The reviewer’s comment: Major Compulsory Revision**

3. The explanation for including mortality among cured and completed cases only for studying long term impact of DOTS strategy is not convincing. Generally mortality reports include all cases and mortality rate reported from this study may not be comparable with results of such studies. I suggest mortality reports (both mortality rates and excess mortality) can be excluded and only recurrence can be reported.

**I respond to the reviewer’s comment as follows:**

Our study objective was to find out what happened to patients with TB after they completed their treatment. We found that patients who have completed treatment or were categorized as cured have excess mortality rates compared with what is expected in this population. In our view, this presents quiet important information for TB control programme. We need more studies on this topic to find out about the causes of death, and thus improve the long term survival of patients after completing their treatment.
We think our research question is scientifically legitimate and methodologically sound. We started with a group of patients who were cured or had completed treatment and followed them for some time to observe the outcome (recurrence and mortality rates) in these group of patients (classical cohort study).

We disagree with the reviewer to exclude this important part of the paper.

**The reviewer’s comment: Major Compulsory Revision**

4. Average duration of follow up is reported as 3.9 years. But majority of patients were followed up for periods less than this average. This can not be called long term follow up. Normally in recurrence studies, cured smear positive cases will be followed up for a defined period of follow up and results reported as % of cases recurred in a specified period of follow up. But this study has differential follow up for different annual cohorts. In this study recurrence rate/100PYO expressed as %/ annum can only be reported.

**I respond to the reviewer’s comment as follows:**

Our study is a cohort study. It is the nature of such studies that they have varying time of follow up. We believe that we have adequately addressed this issue by using suitable statistical methods (Cox regression) to account for the varying degree of follow up.

**The reviewer’s comment: Minor essential revision**

1. The explanation for the query on the survival curve is not clear. My query is not answered. I want to know how many patients were recruited from each year from 1998 to 2006. This information is not furnished. According to the curve farmers and non farmers
were followed up for 9 years. Mention the numbers followed in each group. Do they add up to 725 cases?

**I respond to the reviewer’s comment as follows:**

The number of TB patients recruited from each year and their occupational background is presented below. Date treatment completed was missing for one case.

<table>
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<tr>
<th>Year</th>
<th>1998</th>
<th>1999</th>
<th>2000</th>
<th>2001</th>
<th>2002</th>
<th>2003</th>
<th>2004</th>
<th>2005</th>
<th>2006</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
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<td>30</td>
<td>67</td>
<td>122</td>
<td>117</td>
<td>114</td>
<td>122</td>
<td>110</td>
<td>34</td>
<td>724</td>
</tr>
<tr>
<td>Occupational background</td>
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<td></td>
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<td></td>
<td></td>
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<tr>
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<td>20</td>
<td>47</td>
<td>83</td>
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<td>Non-farmers</td>
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<td>37</td>
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<td>32</td>
<td>37</td>
<td>7</td>
<td>227</td>
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