Author's response to reviews

Title: DOTS improves treatment outcomes and service coverage for tuberculosis in South Ethiopia: a retrospective trend analysis

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Author's response to reviews: see over
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The Editor
BMC Public Health

Re: MS: 947863958585187- 'DOTS improves treatment outcomes and service coverage for tuberculosis in South Ethiopia: a retrospective trend analysis'

Dear Editor,

Thank you for your email of 20th April 2005. We are very grateful for the constructive comments forwarded by the reviewers. We have addressed their comments and have revised the manuscript in line with their suggestions. Below, we have provided a point-by-point response to the reviewers’ comments.

Sincerely,

Estifanos Biru Shargie
Reviewer One: Thomas R Frieden

1. Remove analysis which excludes patients lost to follow up/no record available. These must be assumed to have all defaulted per standard international cohort analysis.

We appreciate the reviewer’s comment and we have now removed all such analyses that exclude patients with unknown outcome. As a result, treatment outcomes are now calculated out of total, not out of patients with known outcome record. Patients with missing outcome record are analysed as defaulters. All figures on treatment outcomes in the text (Treatment results: pages 8-9 & Trend over time: Page 10) and tables 6 and 7 have been adjusted accordingly.

2. Correct grammar, including no “the” before DOTS, extra commas, etc.

Corrected.

3. The fact that 94% of the registrants were new suggests either that there was no anti-TB treatment in the area before, or that there was misclassification of previously treated patients as new. Please comment on this briefly in discussion.

We have included a sentence about this in the discussion (page 13 paragraph 2).

4. Results and discussion should be shortened

We agree with the reviewer that these sections are too long. We have now shortened the results and discussion sections by one-fourth each.

5. Page 14 there are two sentences which require revision. “Increased coverage by SCC alone cannot explain the improvement in treatment outcomes.” This is not supported by the text and it’s not even clear what you are trying to say.

- And “We believe that this is a reflection of gender differentials in access…” Your beliefs should not be part of a manuscript. You can say, “This may reflect gender differentials…” Incidentally, it quite possibly doesn’t, as indicated by the references for the next sentence.

We appreciate the point. We have removed the first sentence and rephrased the second one (page 12 paragraph 2).
Reviewer Two: Marijke Becx-Bleumink

1. This study intends to assess trends in expansion of DOTS and treatment outcomes. In order to assess such trends the authors should describe the trend in DOTS expansion, i.e. year of DOTS implementation in the clinics under study and the treatment outcome in the clinics prior to introduction of DOTS and after introduction. The authors have failed to do so:

`DOTS as a strategy was introduced in the study area in 1996 (Background: paragraph 3 page 3, Trend over time: page 10 1st paragraph). However, it was then initiated in a very few health facilities and eventually scaled up in a phased manner. It took 5 years until all health facilities began to operate under the DOTS strategy (page 10). As a result, our study tries to find out the trend in treatment outcomes during the years prior to the initiation of DOTS (1994-1995) and along the course of expansion of DOTS (1996-2001).`

1.1 treatment results include patients on SCC and patients on LCC for the various categories of patients,

`We presented the results stratified by treatment regimen and patient category in an effort to show the trends in treatment outcomes for various groups of patients.`

1.2 also prior to implementation of DOTS patients were treated with SCC although apparently not daily supervised,

`Yes, some patients were treated with SCC based on certain criteria prior to the introduction of DOTS and we just presented the reality on the ground (Methods: page 3-4).`

1.3 if the objective of the study was to prove that DOTS improves treatment outcome the outcome after DOTS implementation should be compared with that prior to the implementation, while including patients treated with SCC prior to DOTS implementation in the last group. A table of expansion of DOTS over the year, the number of patients diagnosed prior to DOTS implementation after DOTS implementation should be included.

`We appreciate the reviewer’s point. However, our prime objective was not to prove that DOTS improves treatment outcomes as our study design would not allow us to “test” DOTS as a strategy. Our aim was rather to describe the trends in treatment outcome in line with the expansion of DOTS in this particular setting with low health service coverage. I.e. to see if improved treatment outcomes in the area over the study period could be explained by the improved TB service as a result of introduction and expansion of DOTS. The title of the manuscript is a reflection of the conclusion that DOTS worked well in this resource-poor setting- as there is no alternative explanation from the data for the continuing improvement in treatment outcome.`
2. For several analysis data are not presented, including those on treatment outcome of female patients, page 9, of treatment outcome of “return after default” and treatment failures, page 9, and for the analysis made on page 10, first 2 paragraphs, page 11, distribution of patients with missing data, page 12, treatment of small and larger centres, page 13, last 2 lines on patients with unrecorded records.

The data for treatment outcomes of all these groups mentioned above have been presented in percentages rather than actual numbers for fear that including actual numbers in all these sentences would further complicate the text. In addition, we tried to avoid repetitions as numerical data on female, “return after default” and failure patients are presented in table 1 and first paragraph of “Results” section. The statement on the distribution of patients with missing data (page 11) has been taken out in an effort to shorten the manuscript. Treatment outcomes for those treated in small and larger centres are given on table 7.

3. Several statistical analysis are made, however the missing data of substantial groups of patients do not justify this:
- Follow-up smear examinations (table 4) at 2nd 5th and end of treatment were available for 60%, 30% and 21% of new smear-positive patients respectively. Although a decline in positivity rate can be observed, there are too many missing results to draw the conclusions given on page 8, Follow-up.

We agree that follow-up smear examinations were not done for a large fraction of smear-positive patients. We have discussed this issue and its implication in the Discussion section (page 13 last paragraph last 3 sentences). However, there is no reason to believe that patients that had follow-up smear examination done were more likely to remain smear-positive or otherwise. For example, if we look at the trend among patients on SCC (table 4), a fairly large proportion of these patients (range: 63-72%) had a follow-up sputum microscopy and the steady decline in smear-positivity across the years is very evident. The proportion of patients for whom follow-up sputum microscopy was not done did not show much variation from year to year.

-Table 5 and the text on page 8. Treatment results give treatment outcome of 16943 patients, although the heading of the table gives 18,020. Hence results of 19971-16943= 3,028 patients are missing. Table 6 apparently excludes patients with missing information and those transferred out. The same applies to the analysis presented in table 7.

We agree with the reviewer that table 5 does not add up to 18,020 and we have corrected it both in the table heading and the text (Treatment results, 1st paragraph page 8). The number of patients for whom treatment outcome was analysed reduced to 16943 because the analysis was limited to 1994-2000 as a considerable proportion of patients registered in 2001 were still on treatment during the time of data collection (see data analysis 2nd paragraph, page 6).
We have now included patients with missing outcome information and those transferred out in table 6 and the analysis presented in table 7 as per the suggestion (see the revised tables 6 and 7). All patients with missing outcome record are now
assumed to have defaulted from treatment as per the standard international cohort analysis.

4. The presentation under Methods, page 5, 1st paragraph is confusing. The treatment regimens for the different categories of patients under DOTS and non-DOTS areas should be clearly described, e.g. in a table. Criteria for SCC or LCC in non-DOTS areas should be given. There is no mention of a regimen for re-treatment cases, while Ethiopia has adopted the internationally recommended regimen for such cases. From table 3 it appears that retreatment cases are still treated with LCC. The authors should at least have discussed this, because this definitely influences treatment outcomes.

Details of treatment regimens for various categories of patients under DOTS are given in the NTLCP manual, and we have now included the reference. We have included a sentence (page 5) about the criteria used for SCC in non-DOTS areas in the text. We have also included a regimen for re-treatment cases under DOTS (page 5, 1st paragraph). Prior to the full coverage of the treatment centres by DOTS, drug shortage was a big problem in most treatment centres and patients, including re-treatment cases, had no choice but receive LCC. Fortunately, that is not the case at present. As can be seen from table 3, no patient on re-treatment for relapse and failure received LCC in 2000 and 2001. And no patient on re-treatment as a return after default case received LCC in 2001.

5. The data presented in the text are different from those presented in the tables.
   - Abstract, results, 3rd line 57% and 84% should be 62% and 85% (table 6).

   62% and 85% is true for PTB+ on SCC. But when we combine PTB+ on SCC and LCC, the figures would be 57% and 84%. We have now modified the results based on new analysis that doesn’t exclude transferred out patients and patients with no outcome record. The new figures for PTB+ (on SCC and LCC) are 38% and 73% respectively (abstract, page 2; Trend over time, page 10 paragraph 2).

   - Results, 1st paragraph, 14 unknown sex patients not mentioned. The 4th-6th line give 19799 patients in total as compared to 19971.

   14 patients with unrecorded sex are mentioned in table 1. It is true that the sum of those listed in 4th-6th line gives 19799. Because 172 patients (19971-19799) had no category recorded for, and they account for only 0.9% of total (see table 1, patient category).

   - Results, Treatment given, page 7, 1st line, n=7917, while table 3, 1st line gives 7923. 4th line from 7% in 1994 to 59% in 1999 and 99% in 2001 should be 58% in 1999 and 97% in 2001.

We appreciate the comment and we have corrected the figures in the table and the text (page 7, Treatment given 1st paragraph). The first line of the table (SCC) now adds up to 7919.
- Results, Follow-up, page 8, 2nd line n=5112, should be 5009 (table 4), line 4, 93 should be 77 and 2000 should be 1804; line 6, 33/2000 should be 26/#

Corrected. The figure in the text (n=5112) is correct and it included patients with unknown treatment regimen. Table 4 now includes patients with unknown regimen and the figures add up to 5112. Other figures in the text have also been corrected accordingly (table 4 & page 8, 1st paragraph).

- Results, Treatment results, page, 2nd line, 18,020 should be 16,943, the total of table 5. The number of patients in the next lines are different from those presented in table 5.

Corrected.

- Results, page 9, 3rd paragraph, data presented on treatment success among different categories of patients on SCC is different from that presented in the table, 8th line of paragraph 80%, 63% and 74% should be 72%, 63% and 68% respectively.

This analysis was made excluding transferred out patients and patients with missing outcome record. On that basis, proportions- 80% 63% and 74% were correctly calculated. However, we have now removed the whole paragraph based on the reviewers’ suggestion to remove analysis that excludes transferred out patients and those with missing outcome record.

Reviewer Three: David Wilkinson

General
The reviewer’s points are well taken. Outcome analysis has been revised based on the suggestion of the first reviewer, which also was supported by the third reviewer. We have also shortened the text, particularly the results and discussion sections to make it better readable.