Reviewer's report

Title: Risk factors for unsuccessful treatment among new sputum smear positive tuberculosis patients in Yunnan, China

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Reviewer: Syed Tariq

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Comments

This study attempts to identify factors leading to TB treatment failure in rural China. Its strengths are prospective data involving a sizeable patient population. The main new information provided is that family members, and other lay people in the community can act effectively as treatment observers instead of health care workers. However, there are major concerns regarding this report:

As this study looks only at DOTS, I suggest changing the title to ‘Risk factors for unsuccessful directly observed treatment short-course regimen among new sputum smear positive tuberculosis patients in Yunnan, China’.

The authors describe unsuccessful treatment as treatment failure, death or default. Treatment failure can be a) immediate failure with persistence of smear positivity, and b) relapse of TB after apparently successful treatment within a finite period (usually 5 years). It is not clear from this study as to how many patients had lack of response with persistence of smear positivity and how many had a subsequent relapse. Did the patients go through a period of follow-up after completing course of treatment?

The authors state that there is no data available on drug-resistance. This could explain a proportion of treatment failure cases. Some of these cases would fall under the category of relapsed TB with retreatment. This is unclear in this report.

The study targets 26 counties with known high treatment failure rates. Although this is a reasonable approach, there may also be significant differences between these counties and the larger number of other counties showing better outcomes, in terms of levels of education, earnings, health care resources, and public awareness of the services available for diagnosis and management of TB. A comparison, therefore, of failing counties and successful counties could give more valuable insight into factors leading to treatment failure.

The outcome of fewer treatment failures among those who missed doses of <2 weeks as compared to those who did not miss a single dose is unexpected. The authors speculate that this could be due to those who died during the treatment period. To support this statement, the compliance with therapy for those who died should be compared with those who survived.
Although there are 2 tables attached to the manuscript, there are no references to these tables given in the text.

There are several errors in the list of references and refs 10 and 31 are the same.

Table 1 is very large and some of the comparisons given do not add much to the results, such as:

a) breakdown of age into 4 bands, b) income divided into high, medium and low, c) delay in seeking health care broken into <30, 30-59, and >60 days, and d) family attitude categorised as supportive, indifferent and less supportive. The breakdown of these parameters should be simplified as:

- age: <30 vs >30 yrs
- income: low vs medium or high
- delay in health seeking: <30 vs >30 days
- family attitude: supportive vs not supportive

The category for each parameter which is used as control for estimating RR should be given on top preferably in bold, and clarified by a statement beneath the table. This will make the table more meaningful and easier to follow. The obvious controls for different parameters are:

- Age < 30 yrs
- Secondary school or higher education
- Medical insurance – yes
- Income – high
- Co-morbidity – no
- Patient delay < 30 days
- DOT – by healthcare staff
- Baseline sputum smear status <2
- Sputum smear at 2 months – negative
- Side effects – no
- Interruption of treatment – no
- Number of missed doses – none
- Drugs taken as per guidance – yes
- Patient aware of attending CDC for check-ups – yes
- Patient aware of duration of therapy – yes
- Patient realises the need for DOT – yes
- Family attitude – supportive

Each given p value should follow the parameter and its category in question.
Table 2: The parameter of patient delay should be reduced to 2 categories of <30 days and >30 days as there is no difference between the effect of delay of 31-59 days and >60 days. A third column of ‘p value’ should be added, as some of the parameters seem statistically more significant than others.

Other minor points:

Title page
Change ‘the Netherlands’ to ‘The Netherlands’

Abstract
Results, line 4 – change ‘health care seeking delay to ‘delay in seeking health care’

Background
para 1, line 4 – add a reference to the statement, ‘The targets for case detection and treatment success are 70% and 85% respectively’
para 3, last sentence – rephrase as ‘The influence of this approach on treatment outcomes in not known’

Methods
Page 4, para 1, line 1 – change ‘Out of the total’ to ‘Out of a total’
Page 4, para 2, last line – change ‘required’ to ‘taken’
Page 4, para 4, line 8 – change ‘knowledge on TB treatment’ to ‘knowledge of TB treatment’
Page 5, para 1, line 1 – change ‘Information on chest X-ray’ to ‘Information on chest radiograph’
Page 5, para 4, last line – change ‘Yuan equaled’ to ‘Yuan equalled’
Page 5, para 6, last line – change ‘during intensive and continuation phase’ to ‘during both phases’
Page 5, last para – give the name of manufacturer, country and year for the two softwares used.
Page 6, line 4 – change ‘participants and non-participants’ to ‘participants and non-participants in the DOTS programme’

Results
Page 6, last 2 lines – add the actual numbers to the percentage figures
Page 7, 1st para – add the actual figures to all the percentage figures given
Page 7, 2nd para, line 2 – change ‘health seeking’ to ‘seeking health care’
Page 7, para 2, line 3 – I presume the figure of >2+ refers to the average number of bacilli seen under a high power field. If so, this should be added.

Discussion
Page 8, para 1, line 3 – change ‘did know’ to ‘knew’
Page 8, para 1, line 6 – add a ref to the statement ending in ‘18% for Yunnan province in 2007’
Page 8, para 3, last line – change ‘compared for those’ to ‘compared to those’
Page 9, para 1, last sentence – extend this sentence to ‘A prerequisite is that they are trained well, and they remain motivated and committed to the programme’
Page 9, para 3, last sentence – change ‘have’ to ‘has’ and remove the word ‘before’
Page 9, para 4, first sentence – rephrase as ‘Our study has a number of limitations’
Page 9, para 4, last sentence – re-write as ‘non-participation in this study will have biased our findings significantly’

I also suggest a concluding sentence at the end saying ‘More resources and effort are needed to educate the general public to enable them to act effectively as community-based observers of DOT.’

**Level of interest:** An article of limited interest

**Quality of written English:** Not suitable for publication unless extensively edited

**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.