Reviewer’s report

Title: Prevalence of tuberculosis drug resistance in 10 provinces of China

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Reviewer: Abigail Wright

Reviewer’s report:

Dear Authors,

In general I think the paper was well designed and well written with appropriate emphasis on methods and discussion of adjustment of rates and policy implications of high rates of resistance. I enjoyed reading the paper. This model used by China is a good example for other large countries and can be replicated. The comments on the methods section are minor essential revisions and all other comments are really discretionary suggestions for improvement in the paper. Thank you.

GENERAL

In addition to small comments below, it would be nice to see some comments on the survey system itself. Is it costly? Is it useful for trends? What are the strengths and weaknesses in the eyes of the NTP? Have data been sufficient to utilize for policy changes?

ABSTRACT

Results:

-The number indicated, should read 1,405,911,052. The commas in the text appear to be misplaced. Also useful for readers if these isolates correspond to individual patients or if some isolates were induplicate.

-Please specify that retesting for purposes of laboratory quality assurance, for those readers not familiar with TB.

-Why do you think the results changed specifically among retreatment patients, i.e. why were there more DST errors in this group than among new cases. Retested in blinded at the level of lab (as to the treatment history of the patient) so this may require further investigation.

(Authors may want to consider leaving out this last paragraph (staring with However) about adjustment of rates among retreatment cases in 2 provinces. This is not the main point of the paper. It may be more interesting for readers if some drugs required more adjustment than other drugs.

Conclusions:

Authors indicate that although proportion of resistance varies across provinces in China, on average it is high. Please compare to the global average to make this point (4.8%), ref: 4th global report on DRS. Authors may also want to conclude on the importance of a good lab QA system that has been used (as established
in the paper) to check and adjust lab results as required.

INTRODUCTION

-Paragraph one. The authors should use the data from the latest global estimates; 489,139 (95% CIs, 455,093-614,215) MDR cases emerge every year. Reference is the 4th Global Report on Drug Resistance in the World, (WHO/HTM/TB/2008.394), WHO, Geneva, 2008.

-Methods for the estimate of 210,000 MDR cases in China should be described somewhere. Have the authors simply applied the 9.3% estimate and applied it to the estimated number of prevalent cases. If so, please describe in methods section, or briefly in introduction. Are there confidence intervals on this estimate? It would be useful to have them if possible.

-For not TB specialists it is very important to explain in this section the importance of MDR, and to define it. It is also important, in order to situate the conclusions and recommendations to explain XDR-TB and the global situation of DST for second line drugs (that is has only recently be standardized, and magnitude of resistance to SLDs is only beginning to be established as NRLs develop capacity to test second line drugs). The CDC MMWR should be the reference for the revised definition of XDR-TB. The WHO website should have a reference for new recommendations for SLD DST, if not the 4th Global report on DRS can be referenced. And details on the first global survey of SLDs can be referenced as (Shah, N.S., et al., Worldwide emergence of extensively drug-resistant tuberculosis. Emerg Infect Dis, 2007. 13(3): p. 380-7).

METHODS

-Intake of patients. It would be useful to described the reinterview process here. It is mentioned later in the paper following problems with the Liaoning and Henan surveys, but not decribed in detail. The process should be described as well as the date started.

-Laboratory methods: Would be useful to explain the proficiency testing generally takes place before the start of the survey to do a preliminary check on lab proficiency, and retesting during the course of the survey. It would be useful to indicate the full names of the SRLs.

-It would be useful to add a paragraph on data entry, and whether there was double checking.

-Author need to add a paragraph on ethical review, whether or not it was taken up or not. For example, if there is no Ethics review Board in China, authors could explain that in lieu of a national ERB, patients were required to sign a consent form. Or for example, if the surveys were considered a routine aspect of the national TB programme, and were not required to be passed through as ERB this is okay too, but some discussion of the ethical review process should be added.

RESULTS

-Any resistance: Proportions of resistance to H, R, E, S and MDR should be reported. This gives the readers a sense of which drugs are being lost first. If possible to put CIs around the national weighted mean, this would be desirable.
Multidrug resistance: In the last paragraph, please as year of the Liaoning survey also in brackets, just to be consistent.

It should be explained whether proportions of MDR among retreatment cases were also readjusted. And later whether this was taken into account when national weighted means were developed.

DISCUSSION

Liaoning is misspelled in the first paragraph.

It might be interesting to speculate here why adjustment required was greater among the group of retreatment patients. Why was there more DST error in this group, or is it simply related to the smaller sample size. Otherwise, readers may be misled. Theoretically, new and retreatment patients should have the same probability of having a incorrect DST.

It would be good to explain in greater detail as to why the policy of free treatment only for new patients adversely affected the survey., i.e. because patients had an incentive not to disclose their treatment history. This is important both for reasons of correct estimation in the context of a survey but also for patient treatment. This policy should also be discussed, is it still in existence? Etc. Again, the details of rechecking should be discussed in greater detail in the methods section.

To put into context for readers it might be useful to establish what the global average proportion of retreatment cases is. This can be found in the 2008 Global TB Control Report. Then readers know if the proportions in China, are low, average, or high. It may be worthwhile to mention that there is a significant and well established relationship between proportion of retreatment cases in a programme and proportion of MDR among new cases. This was published in the 3rd DRS global report. It would be interesting to see if this holds true for China. In theory provinces with high proportion of retreatment cases should be the same as those with the high proportion of MDR. It is suggested the authors take a look at this and comment if relevant. Both MDR and % retreatment are indicators of programme performance.

There is no mention of drugs on the free market (or available without prescription) is a possible reason for development of resistance. Is this an issue in China? If so, it needs to be mentioned.

DST is misspelled as DTS in the 2nd to last paragraph.

CONCLUSIONS

Conclusions are good and straightforward a further mention on plans for DST to second line drugs will be very useful.

TABLES

The tables are clean and very good. If there is possibility to add confidence intervals for individual surveys this would be desirable.
Level of interest: An article of outstanding merit and interest in its field

Quality of written English: Acceptable

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