Author's response to reviews

Title: Infection control and the burden of tuberculosis infection and disease in health care workers in China: A cross-sectional study

Authors:

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Version: 3 Date: 1 September 2010

Author's response to reviews: see over
Dear Editor,

Thank you very much for your very useful and helpful comments and suggestions.

I revised the manuscript according to the comments and suggestions, and also replied to each reviewer point by point.

Please find the attached replies to each reviewer.

Kind regards, on behalf of all authors,
Guang Xue He
Reviewer's report

Title: Infection control and the burden of tuberculosis infection and disease in health care workers in China: A cross-sectional study

Version: 1 Date: 8 July 2010

Reviewer: kevin L winthrop

Reviewer's report:

Comments: Also, for the authors, I find it strange that the authors give in their results section the difference in LTBI diagnosis between BCG vaccinees and non-vaccinees. Clearly, given they base their LTBI dx on the TST result, it is likely that this difference is attributable to boosting of TST responses among BCG vaccinees. They need to discuss this possibility within their discussion section of the manuscript (currently they don't address this finding in the discussion section, and given they have highlighted it in their abstract, they should).

Reply: BCG vaccination can indeed lead to a false positive result of the TST test. Consequently part of the positive TST results may not reflect the participants’ LTBI status. However, international reviews have reported that the influence of BCG is relatively small in the adult population, especially ≥10 years after BCG vaccination. We have included a discussion on boosting and the potential effect on our findings in the discussion section.

Thank you for your review.
Reviewer's report

Title: Infection control and the burden of tuberculosis infection and disease in health care workers in China: A cross-sectional study

Version: 1 Date: 29 July 2010

Reviewer: Mareli Claassens

Reviewer's report:

Major Compulsory Revisions

1. Add to Introduction: China’s tuberculosis stats (prevalence, incidence, burden), BCG policy and TB infection control policy and the implementation thereof at the time of the study. This should include the occupational TB policy, i.e. screening of HCW at facility level.

Reply: We added the background information in the first and the third paragraph of the introduction section. There was no national TB infection control policy at that time of the study, and also no occupational TB policy, we have added this information to the introduction section.

In China, BCG vaccination is highly recommended by health authorities since the late 1970th and is usually given to all newborns within the first few days of life. We added this information to the methods section.

2. P6 line 6: please explain sample size calculation for 40 randomly selected TB centers. How many of these selected centers had inpatient wards?

Reply: We did not calculate a sample size; we randomly selected two counties from each prefecture of Henan province. We added a flow diagram (Figure 1) to demonstrate the structure of TB control system in Henan province. Fifteen of the selected centers had inpatient wards.
3. P6 line 12: please explain how the checklist was compiled? By whom? How comprehensive was it with regards to TB infection control measures, i.e. did it contain information on administrative, environmental and personal protective measures? How was it validated? Did it include researcher observation within a facility? How does it compare to the CDC risk assessment tool that was published in December 2005?

Reply: This study was completed before the publication of the CDC risk assessment tool. In 2005, NTP mainly focused on the DOTS strategy, and did not start implementing infection control measures. We did not find a relevant assessment tool on TB infection control at that time. In addition, there was no specific guideline on TB infection control in China. Based on the research objectives, the project director invited a few TB control experts including all project members to develop a simple checklist. This checklist encloses some questions on administrative, environmental and personal protective measures. In comparison with the USCDC 2005 checklist, this checklist is much shorter, and most of the questions used different wording. It was tested in the pilot study, and no changes were made to the checklist.

4. P6 lines 12-18: please include the data on the HCW who contracted TB as a separate table, including columns on sputum spear results, culture results, chest x-ray results, symptom screen results as well as category and treatment outcome if possible. Please comment why only three of the cases were smear positive, if possible. Also add data on TST.

Reply: We fully agree with you that the HCW who contracted TB is a very important group. It is difficult to design a well presented table, thus we added information on sputum smear results, chest x-ray results, symptom screen results as well as category in the result section. We informed the patients that they could receive free treatment at the local TB center, but did not follow-up on the treatment results. Due to limited laboratory capacity, we did not conduct culture examination (county/district level facilities do not have the capacity to conduct sputum culture). Because we conducted the chest x-ray screening, we found some TB patients at very early stage with tiny shadows at the chest x-ray, and the majority did not have any symptom. Therefore, only three of the cases were smear positive. We added this information in the discussion section.

5. Please also tabulate/illustrate how many HCW in total were screened symptomatically and by chest x-ray. How many had abnormal x-rays, how many were symptomatic, how many did not give consent or were not available, etc.
Reply: We added this information in the results section.

6. P9 line 14: please comment on the sputum examination room stats – include a recommendation that sputum rooms should be separated from administrative areas (only 15.7 % separated), windows should be open at all times (not only 66.9%) and UVGI should be used daily (not only 66.1%) and tested regularly, especially in the sputum room.

Reply: We fully agree with you that our results on sputum examination room stats indicated that our current sputum room infection control was inadequate. Due to the scope of our research (it covers various departments of the healthcare facility) we chose to place a general recommendation in the discussion section.

7. P11 line 7: the prevalence for HCW working with TB inpatients is 15.9, much higher than any other job location. Please include this in the results/discussion.

Reply: We added this information in the results section.

8. P15 line 3: include administrative measures as first priority to strengthen infection control practices.

Reply: We added the statement on “administrative measures” in the abstract and conclusion.

Minor Essential Revisions

9. P4 line 10: add reference

Reply: We added a relevant reference.

10. P4 line 12: check reference 6 – either change to MDR TB or change reference, insert date
Reply: We changed it to MDR-TB.


Reply: We added the relevant information in text.

12. P5 line 10: ... survey on HCW from TB centers in Henan Province.

Reply: We edited it accordingly.

13. P5 line 13: how does Henan province compare to other provinces with regards to MDR-TB proportion of cases?

Reply: The prevalence of MDR-TB in Henan province is one of the highest in China. We added this information in the study design.

14. P6 line 1: please explain why some TB centers do not have TB clinics? Do these centers have inpatient wards? (could be illustrated in flow diagram, if inserted as advised under discretionary revisions)

Reply: We added a flow diagram (figure 1) in the methods section. The capital of each prefecture includes several districts. All districts have a TB center that is in charge of TB management. TB clinics are available in all prefectures, but a few district level TB centers do not have a TB clinic and inpatient ward. Their patients are diagnosed and treated at prefecture level TB centers. So there were 49 TB centers in Henan province that did not have TB clinics and inpatient wards, and they are only responsible for supervision and monitoring of the TB control program.

15. P6 line 8: Is Zhumadian city in the same province? Please explain why the pilot data were included in the analysis? What was the impact of the pilot study on the protocol?
Reply: Yes, Zhumadian city is in Henan province. The pilot study used the same protocol as the main research, hence was included in the analysis. We mainly gained administrative experience through the pilot study, and did not modify the checklist, the questionnaire, and the implementation procedure after the pilot study.

16. P6 line 14: ... chest x-rays were done on all HCW

Reply: We revised it accordingly.

17. P6 line 15: please explain how the sputum samples were examined. Was this according to the WHO policy at the time?

Reply: Yes, the sputum samples were examined according to the WHO policy at the time. We added this information in the methods section.

18. P6 line 16: please start a new paragraph with: ... A TST was done on all HCW... This was not done on all HCW, but only on the HCW in the preselected facilities. Please explain how many HCW were employed at these selected facilities in total for the time period, of which how many were enrolled in the study?

Reply: We revised it accordingly, and presented numbers in the results section.

19. P9 line 11: Is more information available on the type of pre-employment screening? Was the regular screening program in 48.8% of centers an annual program?
Reply: Our annual screening program is a type of physical examination, which includes chest x-ray, but not TST. In the text, we changed the word ‘regular’ to ‘annual’ screening.

20. P10 line 5: what was the definition of ‘large TST indurations’?

Reply: Large TST induration refers to induration ≥15mm. This information was also added in text.

21. P10 line 11: define which job cadres were included in ‘job location within the TB center’?

Reply: We included all job cadres in job location within the TB center, including doctor, nurse, X-ray technician, laboratory technician, pharmacist, register staff, administrative staff, project officer, DOT supervisor and logistic staff. The specific job cadres within each job location are listed below:

- Administrative/logistic department: medical administrative staff, general office staff, accounting staff, and logistic staff;
- TB outpatient clinic: doctor, nurse, and register staff;
- TB inpatient ward: doctor, nurse;
- supervision and monitoring department: TB management staff, DOT supervisor, project officer, statistician;
- Pharmacy: pharmacist;
- X-ray department: X-ray technician;
- Laboratory: lab technician.
As this information is out of our research scope, we did not add it in the text.

22. P10 line 12: which are the ‘medical staff’ and which are the administrative staff?

Reply: Administrative staff refers to those who work in the general office, medical administrative office and the office of the directors. Medical staff refers to people who work in the TB outpatient clinic, TB inpatient ward, TB program supervision and monitoring department, pharmacy, x-ray department, and laboratory. We expect this does not need an explanation for the readers and did not add this information in the manuscript.
23. P10 line 14: which factors were similar for HCW when those with and without BCG scars were compared? (list factors)

Reply: The factors included age, job location, duration of employment, inpatient ward, and level. We added this information in the result section.

24. P11 line 2: HCW who worked longer than 10 years at the facility had a lower prevalence than those employed 5-9 years. Please comment.

Reply: Although HCW who worked longer than 10 years at the facility had a lower prevalence than those employed 5-9 years, this difference was not statistically significant (p>0.05). One possible explanation is that we included a small number of TB patients in this study. As shown in table two, LTBI rate was higher among HCW who worked longer than 10 years than those employed 5-9 years.

25. P11 line 4: please include the total number of females here, so that the reader realises 9/1937 cannot be significant.

Reply: We added the total number of females in the text.

26. P11 line 17: include data from prevalence survey in 2000. Are the prevalence data for the same age groups, geographical location etc.?

Reply: We included the data from prevalence survey in 2000 in the first paragraph of the discussion section. Our study used the same age groups, but only covered one province. The survey in general population in 2000 covered the entire country.

27. P12 line 8: please clarify – does the phrase “an average LTBI prevalence of 54%” refer to the general population in China? If not, please include data on the LTBI prevalence in the general population of China.
28. P12 line 13: please comment why HCW working at prefecture level were at higher risk for developing TB?

Reply: At prefecture level, all TB centers had TB clinics and inpatient wards. But at county level, only some TB centers had TB clinics and inpatient wards. Patients with more severe TB disease may choose prefecture TB center to seek medical care, which may increase the exposure to TB at prefecture level. We added this information in the text.

29. P12 line 16: please include data to confirm statement “we did not observe the association of male sex with increased M.tb infection risk”.

Reply: Using male sex as the reference group, the OR was 1.1 (95% CI: 0.9-1.3). This result was also added in the text.

30. P13 line 8: which TB infection control standards are referred to?

Reply: We referred to the WHO TB infection control standards, and added this reference in the text.

31. P13 line 9: please include references to suggest that these interventions would be ideal for this context? Were these interventions evaluated as part of the checklist?

Reply: We added the reference in the text. The interventions were not evaluated as part of the checklist.

32. P13 line 13: are exhaust ventilation systems feasible in this rural area? Will maintenance not become an issue?
Reply: Implementation and maintenance of simple ventilation systems, such as the exhaust fan, might be feasible at county level.

33. P14 line 13: please explain the assumptions for this calculation.

Reply: In our study, medical staff (LTBI prevalence=56%) and administrative/logistic staff (LTBI prevalence=42%) worked in the same facilities. So the calculation was done as \((56\%-42\%)/56\%=25\%\). We added this information in the text.

34. P14 line 20: how generalisable are the data to other provinces in China?

Reply: It is the first study about TB infection and disease among Chinese HCW. In China, TB infection control was at a very early stage at the time of the study. So the TB infection control situation in most areas of China was likely to be similar to Henan province. Therefore, we think the data is generalisable to other provinces in China. We added this information in the discussion section.

35. P25 table 3: please speculate on why 14 of the 20 TB-cases were found in the sample population?

Reply: Investigations for TB disease was done in all 127 TB centers while TST was done in a subset of 58 TB centers. In total in the 127 centers, 20 TB cases were detected, 14 out of those were from the subset of 58 centers.

36. Spelling, grammar mistakes and abbreviations to be corrected throughout the manuscript. References and format to be checked (see reference 2, 17...)

Reply: We carefully corrected the spelling, grammar mistakes and rechecked the abbreviations and references through the entire article.

Discretionary Revisions
37. P 4 line 14: insert flow diagram to illustrate breakdown of TB programme in Henan province

Reply: We added a flow diagram (Figure 1).

38. Please insert reference number for ethics approval by Chinese Ethics Committee.

Reply: This study was the research project (035) of the World Bank/Department for International Development (WB/DFID) China Tuberculosis Control Project, which was approved by the Chinese Ethical Committee for TB Operational Research in Beijing. No reference number is given out by the Chinese Ethical Committee.

39. P9 line 18: is there any information available on where the UV lights were situated? Current literature favours upper room UVGI.

Reply: Yes, the UV lights were situated at upper room level. This information is added in the result section.

40. Please consider including data on TB/HIV in China. Specifically about HIV in HCW, if any known data are available.

Reply: Currently, there is no reported data about TB/HIV in China.

41. P11 line 15: consider adding the phrase: “... TB infection control as evaluated by this checklist/study... “. Data on the administrative components of TB infection control were not included in the manuscript, so TB infection control in general can not be commented on.

Reply: We revised the text accordingly.
42. P11 line 19: for this part of the analysis, consider using a 6 mm cut off for the study participants as well.

Reply: Our study is consistent with most international studies that also used 10mm as a cutoff point. In the discussion, we compared our findings with the national 2000 survey in the general population which used the 6mm cut-off point. It showed that the LTBI prevalence of 56% among medical staff was higher than the LTBI prevalence of 47% (using a cut-off point of 6 mm) in the population group of 15 years or older from the survey in 2000.

43. Please consider including an argument explaining why LTBI rates were similar to that of the general population, but TB-disease rates were much higher.

Reply: The general population data was taken from the 2000 survey, which was five years prior to this study. The 2000 survey used 6mm as the cutoff point. The LTBI rate (56%) was still higher than our result (47%). The TB disease rate was much higher than the 2000 survey. It is because the 2000 survey used a different TB disease assessment tool chest fluoroscopy, which had a much lower sensitivity than the chest X-ray method that was used by our study. Because we conducted the chest X-ray screening, we found some TB patients at very early stage with tiny shadows at the chest x-ray, and the majority did not have any symptom. We added this information in discussion.

44. P13 line 18: please include the study dissemination strategy.

Reply: We will report the key research findings and recommendations at the annual NTP meeting and national TB infection control meeting. We did not include this information in the text.

45. In the discussion, please try to follow the tables’ variables from top to bottom and comment on all variables. Please look at the formatting of table 2 (inpatient ward and size of clinic)

Reply: We adjusted the formatting of Table 2.
Thank you very much for your very careful review! We truly appreciate your useful and helpful comments and suggestions.
Reviewer's report

Title: Infection control and the burden of tuberculosis infection and disease in health care workers in China: A cross-sectional study

Version: 1 Date: 11 August 2010

Reviewer: Wendy A Cronin

Reviewer's report:

Review – authors

Thank you for the opportunity to review this manuscript. The authors conducted a carefully executed cross-sectional study of latent tuberculosis (TB) infection and TB disease among health care workers in Henan province, China, where MDR-TB rates are high. Infection control practices were poor to nil. Authors found that older workers, workers with a longer duration of employment, and workers at TB centers and inpatient units had higher rates of latent TB infection. TB disease rates among health care workers were nearly 3 times greater than among administrative staff.

While more global attention needs to be focused on strengthening TB infection control measures such as availability of N95 masks, proper environmental actions, and employee and patient training, I do not believe this manuscript adds to the current body of knowledge. In addition, the study is 5 years old (2005), and the findings regarding infection control practices may be out of date for Henan Province, China.

Reply: There is no information of Chinese TB infection control in the international scientific literature. Therefore, we think that our study is valuable even though the study was done in 2005. Moreover, this would be the first study documenting the prevalence of LTBI and TB disease among HCW in China in the international scientific literature.

Specific comments:

1. Page 5, Study design: Suggest providing background TB risk information about Henan province (such as % MDR-TB) in your introduction. No need to justify in Methods.
Reply: we removed the background information on (TB in) Henan to the introduction section.

2. Page 5-6, Study population and sampling: This section could be summarized.

Reply: We shortened the study population and sampling section. The remaining information is provided to help the readers have a better understanding about the unique structure of the Chinese provincial TB control system.

3. Page 7, Quality control: this section nicely demonstrates careful planning and study execution.

Reply: Thank you.

4. Page 11, Results: The division of groups (female, male smokers, male non-smokers) is understandable. However, please report in the text the proportion of females who smoke.

Reply: we added the percentage of female smokers in text.

5. Page 11, Discussion: First paragraph can be summarized. You do not need to repeat detailed findings in the discussion. The last sentence is useful, as it adds to the results data.

Reply: We deleted some information. We choose to keep the figures in this paragraph to compare with the general Chinese population based on the 2000 national survey report. These comparisons were not included in the result section.

6. Page 13, first paragraph: Older hospitals in Peru were shown to have greater ventilation than a modern building with mechanical ventilation. You do not address this when you mention older buildings.
Reply: The older building construction in China is very different compared to Peru. In China, older buildings generally do not have separate departments, and are relatively closed. Especially in the Northern part of China, the windows and doors are closed most of the time.

7. Page 13, first paragraph: Suggest you would have a more informative study if you compare current practices and results with your results in this project. What interventions have been conducted and did the TB infection and disease decline?

Reply: Up to this date, TB infection control is still at very early stage in China. In most areas, TB infection control interventions have not been implemented.


Reply: Thank you.

Thank you very much for your review.
Reviewer's report

Title: Infection control and the burden of tuberculosis infection and disease in health care workers in China: A cross-sectional study

Version: 1 Date: 1 August 2010

Reviewer: Ashwin Dharmadhikari

Reviewer's report:

Major Compulsory Revisions

None

Minor Essential Revisions

1. It would be important to report how many HCW were eligible for the study, but did not consent to participate or were not available to participate. In addition, if the authors have any information, or hypotheses, about the reasons for non-participation among the non-participants, this too would be important to include and discuss. For example, in paragraph 1 of the section called “LTBI prevalence” the authors note that the TST was employed in 2153 (94.1%) of 2288 HCW in the 58 selected TB centers. Any explanations or speculation about the 6% on whom TST was not employed? This information will help the reader understand whether the data presented in this manuscript reflect information pertinent to the entire population of HCW, or just a subset that agreed to participate in the study. It will also help support the extent to which these data are generalizable to HCW in China.

Reply: TST was not taken in 135 (5.9%) out of 2288 HCW. The explanations include: 51 did not go to work on the day of TST, 30 had TST but did not show up on the result reading day, 20 were on holiday, and 34 refused to do TST. We think 94.1% is a high participation rate, and reflects the general HCW population. We added this information in the results section. Also, we added information on reasons why 13 HCW were not screened for pulmonary TB disease.

2. Table 2 (and the manuscript text referring to Table 2): The authors must tell
the readers the variables for which the crude ORs were adjusted to arrive at the “Adjusted OR” for each analysis. Otherwise, we as readers do not know what the adjusted ORs represent.

Reply: We adjusted for all the other factors listed in Table 2. We added this information in the text.

3. Introduction, Paragraph 2: The authors state that “Health care facilities in China do not routinely perform tuberculin skin tests (TST) on HCW because endemic TB transmission and cross-reactivity with BCG after vaccination might lead to non-specific reactions to TST”. The way this is written, it suggests that endemic TB transmission might lead to non-specific reactions to TST. In fact, endemic TB transmission would not result in non-specific TST reactions, but may reflect actual TB infection. The sentence should be reworded to convey the point, which I presume the authors wish to make, that health care facilities in China are not doing TSTs on HCW because endemic TB transmission may reduce the utility of using the TST as a marker of nosocomial TB transmission.

Reply: We agree with your point. We revised this paragraph and then decided to leave this point out.

Discretionary Revisions

1. Table 2: Authors should also mention in the label for Table 2 that this table includes the basic demographic data on their HCW cohort. In addition, it would also be great to put a sentence in the text of the manuscript about the demographics (average age, gender breakdown, etc.) of the HCW cohort.

Reply: We added the relevant demographic information in the result section.

Thank you very much for your very careful review.