Author’s response to reviews

Title: Evidence for heterogeneity in China’s progress against pulmonary tuberculosis: uneven reductions in a major center of ongoing transmission, 2005-2017

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Version: 1 Date: 21 Mar 2019

Author’s response to reviews:

Dear Dr. Torres,

Thank you for allowing us to revise and resubmit our manuscript “Evidence for heterogeneity in China’s progress against pulmonary tuberculosis: uneven reductions in a major center of ongoing transmission, 2005-2017” for further consideration by BMC Infectious Diseases (INFD-D-19-00048). We appreciate the constructive suggestions provided by the reviewers, which have helped to substantially strengthen the manuscript.
We have revised the manuscript according to the reviewers’ comments and suggestions, and we submit a revised version along with point-by-point responses to reviewers’ concerns.

We look forward to hearing from you regarding our revision, and we would be glad to respond to any further questions or comments that you or reviewers may have.

Our sincere regards,

Drs. Qu Cheng, Justin Remais and Jin’ge He (on behalf of all authors)

Reviewer 1: nicely designed study and well written manuscript too

We greatly appreciate the reviewer for their evaluation of the work and their supportive remarks.

Reviewer 2: I would like to apology for the delayed report. Overall, it is an informatively descriptive study on PTB.

We thank the reviewer for their overall positive assessment of the research.

1. Although the authors described the temporal and spatial patterns of PTB in detail, I expect to see more inferential statistics associating risk factors with these patterns.

We appreciate the reviewer’s comment, and agree that further work is needed to better establish the determinants of the epidemiologic patterns that our analyses revealed. We ourselves have plans to investigate in greater detail the specific risk factors that underlie the patterns we describe in the present work. For this manuscript, we undertook several major challenges that will in fact enable future research to pursue such analyses. For instance, estimating annual PTB notification rates and the spatiotemporal distribution of PTB incidence in the region was a major undertaking, requiring nearly two years of collaborative research among epidemiologists, database developers, spatial statisticians, and public health workers. Detailing the demographic, temporal, and spatial distributions of active and smear-positive PTB cases reported from 2005 to 2017 is a critically important contribution to the research in its own right. In the revision, we have improved our discussion of key risk factors—including temperature, ultraviolet radiation, PM2.5 level, HIV status, GDP, etc.—that underlie the temporal (see page 12, paragraph 1) and spatial (see page 12, paragraph 2) patterns of PTB. We agree with the reviewer that future research should pursue these risk factors and others in greater detail, and in the revision we state as much at the end of the discussion (see page 13, paragraph 2).

2. Distribution of PTB reporting facilities (Figure 6): I am confused about the purpose of releasing this information. As the map presents, the frequency of facilities is
disproportional by year. Therefore, could this facility factor (like misclassification among regions) affect the spatial distributions and trends of PTB cases from 2005 to 2017?

We appreciate the reviewer’s point, and controlling for the effect of increasing reporting facilities on the spatial distribution and trend of PTB cases was our thinking exactly. We have explained our motivation on page 6, paragraph 3 and page 13, paragraph 1. Since we observed sharp increases in reported incidence rate of active PTB in western Sichuan, which coincide with the area where the sensitivity of surveillance was increasing, we wondered if the observed increase in incidence rate was an artifact of ongoing enhancements in reporting coverage and quality. We used reporting facility density as a proxy variable to control for surveillance sensitivity, and found no significant correlation between the growth rate of reported incidence rates and reporting facility density (see page 10, the end of paragraph 2). We also detail the limitations of our approach in the discussion, such as our assumption that all reporting facilities perform equally (see page 12, paragraph 3). To help readers better understand our motivation for the reporting facility analyses, we have added discussion in the revision (see the beginning of page 8, paragraph 4) showing the distribution of reporting facilities, and clarifying the purpose of this analysis.

Misclassification among regions should be rare in our study, given that we conducted the analyses at county-level, and current health insurance programs in Sichuan only cover expenses in healthcare facilities located within the same county as the subscribers’ residential addresses.

3. Hot spots of PTB (Figure 7): any explanations regarding the hot spots? Any policy implications on these findings?

We appreciate the reviewer’s queries. We have revised our discussion of the persistence of clusters of ongoing transmission in eastern Sichuan, an area with low GDP per capita, limited access to healthcare, and the presence of major transportation hubs (see added Supplementary Figure 7). We also discuss the clusters identified in western Sichuan where low GDP per capita is also an important risk factor, as is ethnic minority status (see page 12, paragraph 2). Finally, we have also added discussion in the revision regarding the policy implications of our findings, such as the need to direct more resources to control and surveillance activities in western Sichuan, where the prevalence of HIV/AIDS is high and the reported incidence rate is increasing; and also the need to build improved laboratory capacity in areas where clusters can be identified among active PTB cases, but not smear-positive PTB cases (see page 13, paragraph 2).