PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Tuberculosis treatment management in primary healthcare sectors: a mixed-methods study investigating delivery status and barriers from organizational and patient perspectives
AUTHORS	Zhou, Jiani; Pu, Jie; Wang, Qingya; Zhang, Rui; Liu, Shili; Wang, Geng; Zhang, Ting; Chen, Yong; Xing, Wei; Liu, Jiaqing; Hu, Daiyu; Li, Ying

VERSION 1 – REVIEW

REVIEWER	Pradipta, Ivan Padjadjaran University, Pharmacology and Clinical Pharmacy
REVIEW RETURNED	08-Jan-2022

GENERAL COMMENTS	The authors attempted to analyze the current status of TTMS and its barriers faced by health care providers from the perspective of the organization and TB patients. The idea is really good to improve TB services in the study setting. However, the design needs more attention to have a robust estimation. Data representativeness to the targeted population and the sampling strategy are essential in the quantitative study. It is unclear how the minimum sample size was defined and whether the participant represented the targeted population. In the quantitative instrument, It is still unclear whether the questionnaire is valid and reliable since there is no detailed information in the validation part. I also identified that participant selection in the qualitative study was not based on the specific criteria/characteristics that guide the researcher to select the appropriate participant. Maximizing participant characteristics that can affect TTMS delivery should be considered in selecting participants in the qualitative study. Selecting participants in the group of poor TTMS delivery from the quantitative study will also help the authors explore the factual barriers of TTMS in the qualitative study. Using only two TB patients participants is difficult to define saturated information from the patient perspective. Furthermore, data integration from the quantitative and qualitative studies should be described clearly in the mix-method design. Please kindly other comments/questions that may improve the manuscript: Please use the updated global TB report (e.g., in line 72) Line 162, how many percentages of the response rate participant Line 157-168, the number and reasons of excluded participants should be reported

	Line 238, how do you ensure that the number represented the targeted population?. Please provide a flow diagram of the participant recruitment (see strobe guideline).
	Line 185, are there any specific criteria for the purposive sampling?
	Line 185, it is really hard to identify saturated information from only 2 TB patients participants to analyze from the patient perspective
	Line 181, it is important on how the credibility information can be obtained in the qualitative study
	Line 211, it should be reported how many missing data in the analysis process
	Line 214, what do you mean with TTMS delivery 90%? Are there any criteria and standard activities? It should be stated in the operational definition of this study
	Line 218, the data should be ensured to fulfill the logistic regression assumption
	Line 222, "creating theoretical framework," seems the author uses an inductive analysis. However, in line 225, the authors stated that the framework had been defined into four domains that showed this study used deductive analysis. Please clarify which one did you use
	Line 238. The number of participants should be ensured whether the number represents the target population
	Table 1. it is unclear whether this is multi- or bi-variate analyses

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Dr. Ivan Pradipta, Padjadjaran University

Comments to the author: The authors attempted to analyze the current status of TTMS and its barriers faced by health care providers from the perspective of the organization and TB patients. The idea is really good to improve TB services in the study setting. However, the design needs more attention to have a robust estimation. Data representativeness to the targeted population and the sampling strategy are essential in the quantitative study. It is unclear how the minimum sample size was defined and whether the participant represented the targeted population. In the quantitative instrument, it is still unclear whether the questionnaire is valid and reliable since there is no detailed information in the validation part. I also identified that participant selection in the qualitative study was not based on the specific criteria/characteristics that guide the researcher to select the appropriate participant. Maximizing participant characteristics that can affect TTMS delivery should be considered in selecting

participants in the qualitative study. Selecting participants in the group of poor TTMS delivery from the quantitative study will also help the authors explore the factual barriers of TTMS in the qualitative study. Using only two TB patients participants is difficult to define saturated information from the patient perspective. Furthermore, data integration from the quantitative and qualitative studies should be described clearly in the mix-method design. Please kindly other comments/questions that may improve the manuscript:

1. Comment: Please use the updated global TB report (e.g., in line 72)

Response: We gratefully appreciate for your valuable comment. We have revised the first paragraph in the introduction section by using the updated World Health Organization global TB report (2021). We have also revised the description of the TB epidemic in China by using the updated data. The corresponding references have been revised. Thanks again for your careful check. (Main document: Line 65-77, page 4)

2. Comment: Line 162, how many percentages of the response rate participant

Response: Thank you for your rigorous consideration. In the quantitative study, a total of 261 TB HCWs and 481 TB patients were recruited to participate in the survey, of whom 0 HCWs declines (response rate was 100.0%), 16 TB patients declined and 6 <15 years old were excluded (response rate was 95.4%). Finally, 261 TB HCWs and 459 TB patients were included in the analysis. We have added a description of the percentages of participant response rate in the methods section. Thanks again for your valuable comment. (Main document: Line 173, Line178, page 9)

3. Comment: Line 157-168, the number and reasons of excluded participants should be reported

Response: We gratefully thanks for your suggestion. For the patient-participants, a total of 481 TB patients were recruited to participate in the survey, and 16 declined. Six TB patients <15 years old were excluded, and finally 459 TB patients were included in the analysis (response rate were 95.4%). For the HCW-participants, a total of 261 TB HCWs in the selected counties/distracts. Finally, all 261 TB HCWs were recruited and welling to participate in the survey, and zero declined (response rate was 100.0%). We have added this description in the methods section. Thank you again for your kind suggestion. (Main document: Line171-173, page9)

4. Comment: Line 238, how do you ensure that the number represented the targeted population? Please provide a flow diagram of the participant recruitment (see strobe guideline).

Response: We gratefully appreciate for your rigorous consideration. The sample size for patient-participants was estimated using Kish and Leslie formula as follows: $n=Z_\alpha^2\, p\, (1-p)/d^2$ where: n= minimum desired sample size. Z_α = the standard normal deviate, usually set as 1.96 which corresponds to 5% level of significance. P = the average rate of tuberculosis treatment management was estimated based on the available literature, and its value was set at 37.1%. d = degree of accuracy (precision) set at 5% (0.05). Therefore, the calculated minimum sample size for TB patients was 359 ($n = 1.96^2 \times 0.371 \times (1-0.371)/0.05^2 = 359$). A total of 481 TB patients were recruited to participate in the survey. Finally, there were 459 TB patients met the inclusion criteria and completed the survey (response rate were 95.4%). The stratified random sampling method was used to select study sites based on socioeconomic developing status. All counties/districts in Chongqing municipality and Guizhou province were grouped into three levels according to the per capita GDP. A total of 12 districts/counties were included in this study. All the primary healthcare sectors in the 12 selected counties/districts, totally 71 PHC sectors were included in this study. Then, all TB HCWs at the selected 71 PHC sectors were all involved in the survey. We have added this description and corresponding references in the methods section. We have also added a flow diagram of the participant recruitment below. Thank you again for your kind suggestion. (Main document: Line 165-179, page 9)
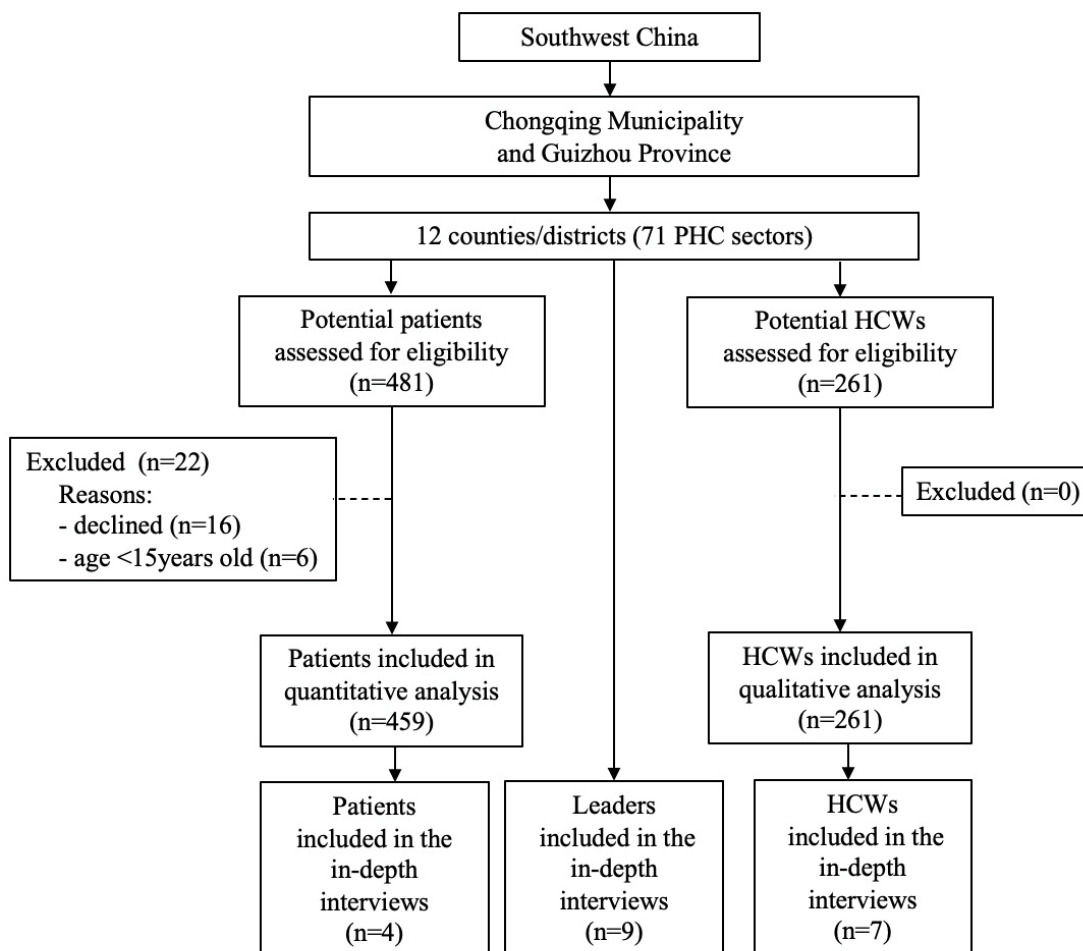
Figure: the flow diagram of the participant recruitment

5. Comment: Line 185, are there any specific criteria for the purposive sampling?

Response: We gratefully appreciate for your careful check. Purposive sampling method was used to selected participants with different background, age, and experiences related to TTMS in this study. Therefore, in-depth interviews were conducted with: HCWs from the PHC sectors of different socioeconomic levels who had delivered TTMS for at least one year during the study period; leaders from the local CDC and the Health Commission who were responsible for TB control program during the study period; and patients from regions of different socioeconomic levels who had received TTMS and were about to end their TB treatment during the study, which ensured patients had sufficient experiences related to TTMS. We have added this description in the methods section for better understanding. Thanks again for your valuable suggestion. (Main document: Line 194-206, page 10)

6. Comment: Line 185, it is really hard to identify saturated information from only 2 TB patients participants to analyze from the patient perspective

Response: We gratefully appreciate for your rigorous consideration. To increase the saturation of qualitative findings, we have added the results of 2 TB HCWs and 2 multidrug-resistant TB (MDR-TB) patients on the basis of the original qualitative results in the "revised manuscript" last May. The original intention of the previous revised manuscript was to reword the Ethics Approval statement and add the Patent and Public Involvement. We are very sorry that you did not see this revised manuscript due to our problem during the upload file operations. Currently, our qualitative data included the in-depth interviews of 9 leaders, 7 TB HCWs, and 4 TB patients. Among the 4 interviewed patients, 2 drug-sensitive TB (DS-TB) and 2 MDR-TB respectively, all of them completed anti-TB therapy (6-8 months therapy for DS-TB TB, and 24 months therapy for MDR-TB). We have revised the description in the results section and in table 5. Thanks again for your rigorous consideration. (Main document: Line 305-311, page 15)

7. Comment: Line 181, it is important on how the credibility information can be obtained in the qualitative study

Response: We gratefully appreciate for your rigorous consideration. We have added the description of how we ensure information's trustworthiness and credibility in the method section. Thank you again for your kind suggestion. (Main document: Line 209-220, page 11)

8. Comment: Line 211, it should be reported how many missing data in the analysis process

Response: We gratefully appreciate for your rigorous consideration. We added number of missing data: when analyzing gender, age, medical school education, of HCWs, major, professional title, number of BPHS programs undertook, monthly income and working satisfaction etc., only 259, 249, 247, 256, 240, 225, 242 and 259 HCWs respectively responded those questions in survey, and so we deleted the HCWs who did not responded this question. (Main document: Line 245-250, page 12-13)

9. Comment: Line 214, what do you mean with TTMS delivery 90%? Are there any criteria and standard activities? It should be stated in the operational definition of this study

Response: We gratefully appreciate for your rigorous consideration and valuable suggestion. We have added the definition in the method section. Thanks again for your kind suggestion. (Main document: Line 280-283, page 14)

10. Comment: Line 218, the data should be ensured to fulfill the logistic regression assumption.

Response: We gratefully appreciate for your careful check. Factors associated with lower delivery rate (<90%) screened by the Chi-square test (p<0.05) were then entered into multivariate logistic regression models (delivery rate <90% = 1, delivery rate >90% = 0), which were used to examine the effects of those factors on TTMS delivery. The Chi-square test results were placed in Appendix 1. Thank you again for your rigorous consideration. (Main document: Line 250-256, page 13)

11. Comment: Line 222, "creating theoretical framework," seems the author uses an inductive analysis. However, in line 225, the authors stated that the framework had been defined into four domains that showed this study used deductive analysis. Please clarify which one did you use.

Response: We gratefully appreciate for your rigorous consideration. We used deductive analysis. The theoretical framework we utilized is called the Practical Robust Implementation and Sustainability model (PRISM). This model considered how the intervention design, recipients, external environment, and implementation and sustainability infrastructure influence health program implementation and success, which widely used as theoretical framework in implementation research. The adaptation of PRISM for this study is illustrated in Figure1. Thanks again for your kind suggestion. (Main document: Line 262-267, page 13)

12. Comment: Table 1. it is unclear whether this is multi- or bi-variate analyses

Response: We gratefully appreciate for your careful check. We prepared an Appendix 1, which shows the results of univariate analysis of factors associated with TTMS with lower delivery rate by using the

Chi-square test. And the table 4 in the manuscript shows the results of multivariate logistic regression analysis of factors associated with lower delivery rate of TTMS by HCWs. We have reworded the title for tables to make it clearer. Thank you so much for your kind comment. (Main document: Line 345, page 21)

Point-by-point response for explaining other changes in the manuscript (the line number corresponds to "Main Document-marked copy"):

1. Line 28, we corrected the number of questionnaire for TB HCWs and TB patients.

2. Line 29, as we added four more in-depth interviews in the results, we have revised the description in the abstract section.

3. Line 30, we have revised "HCW" and "patients" into "TB HCWs" and "TB patients".

4. Line 32, we have revised the study setting from "West China" into "Southwest China" to provide a more specific description.

5. Line 35-45, we have revised some grammar issues.

6. Line 110-116, we moved the sentence to the "Definition" in the methods section.

7. Line 121-124, we moved the sentence to the "Definition" in the methods section.

8. Line 141-144, we reworded this paragraph.

9. Line 146-182, we have revised the study setting section with update data.

10. Line 195, we reworded "TB dispensaries" into "local OHC sectors" to provide more specific description.

11. Line 222-226, we reworded "such as" into "e.g.,".

12. Line 276, we added more specific description for "local language".

13. Line 336-349, we added "(n=)" after each percentage to provide more specific description.

14. Line 360, we reworded the title of table 1.

15. Line 400, we have revised the table 5 for updated presentation of the qualitative results.

16. Line 621, we revised the reference section with updated versions.