PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Knowledge and practice of health workers about control and prevention of multidrug-resistant tuberculosis in referral hospitals, Ethiopia: A cross-sectional study
AUTHORS	Alene, Kefyalew Addis; Adane, Akilew; Yifiru, Sisay; Bitew, Bikes; Adane, Aynishet; Koye, Digsu Negese

VERSION 1 – REVIEW

REVIEWER	RUTH DIVINE AGUSTIN University of the Philippines - Manila, Department of Medicine, PHILIPPINES
REVIEW RETURNED	27-May-2018

GENERAL COMMENTS	How the participant were "randomly selected" was not elucidated in Methods sections. There was mention of the development of the questionnaire by "a team of health workers" but it was not specified whether or not the research team or an independent group was involved. Specifics on the questionnaire used should be mentioned (e.g. what choices for each question, how the correctness of each answer was determined, how knowledge and practice were categorized as poor or good, etc). In terms of the statistics, it was not explained why a p-value of 0.2 was used.

REVIEWER	Nebiyu Hiruy Management Sciences for Health, Challenge TB project, Ethiopia
REVIEW RETURNED	16-Jun-2018

GENERAL COMMENTS	Study setting: the author has to explain how he selected the two hospitals out of the total hospitals Data collection instrument: Lacks details on the process followed to prepare the data collection tool. How did the authors ensure validity of the instrument? What actions were taken? I would like to see the data collection tool. How are the study participants selected? All of the above need to be described. The cut off points for the study outcomes are not outlined. Example: Knowledgeable? There are some editorial issues: some of them, Page 6, line 1-10 there are editorial issues Page 7, line 25 editorial issue…participants Page 7, line 40 editorial issue…wards More detailed feedback can be provided based on your response.

REVIEWER	Michael E Thompson

	UNC Charlotte, USA
REVIEW RETURNED	20-Jul-2018

GENERAL COMMENTS	To the Editor(s): Below is my review of the Knowledge and practice of health workers about control and prevention of multidrug-resistant tuberculosis in referral hospitals, Ethiopia manuscript The manuscript addresses the increasingly critical issue of nosocomial MDR-TB via a cross-sectional study of provider knowledge and self-reported practice in Ethiopia. The manuscript is of modest interest and importance, documenting that the state of affairs in Ethiopia is comparable to much of the world. The cross-sectional, nonrandom sampling design limits the analytic value of the sample beyond descriptive statistics. In addition, the document is poorly edited, with omitted and added words and transposed words (e.g., words instead of wards, note instead of not, forth instead of fourth) sprinkled throughout the text and tables. Recommendation: Consistent with my structured review below, my recommendation is REJECT (MAJOR REVISION) Title: The title is adequate. Abstract: [Minor concern] The abstract contains several editorial errors (missing or added words), but otherwise effectively summarizes the manuscript. Body: [Minor concern] As noted for the Abstract, the body is not tightly edited. Introduction: The introduction provides a concise, well-referenced summary regarding MDR-TB globally and in Ethiopia. Methods: [Moderate concern] The methods, while rudimentary, are appropriate to establish a working estimate of provider MDR knowledge and practice, but the convenience sample, as tersely described, unduly limits confidence in the representativeness of the findings. Furthermore, the rigor/validity of the knowledge assessment instrument is not well developed, nor is a rationale for using a relativistic measure (the mean) rather than an objective threshold score to determine “good knowledge,” especially as the results presentation (P7 lines 1-5) implies knowledge of some items was deemed more important than other items. Results: [Major concern] The socio-demographic profile lacks benchmarking between the respondents and the overall provider population. Furthermore, the referenced Table 1 (P6, line 44) does not contain the information expected (a missing table?). The body of the manuscript and/or the Table 1 referred to on P7 would benefit from indicating the average total number of correct items to provide a referent for where the poor/good knowledge distinction was made. That information is not evident from the solely item-level presentation.

	[Moderate concern] The reasoning for presenting AOR only for education (and which variables were adjusted for) in Table 2 is unclear given the limited description in the methods section. [Moderate concern] The language used in describing self-reported practices makes it sound like it has accurately captured actual practice. [Major concern] Good practice is never defined and items responses not reported, limiting the value of this passage. Discussion: The discussion, though limited by the weaknesses in the underlying analysis, is adequate. Conclusions: [Major concern] Since poor knowledge was defined relativistically (being below the mean), the authors have no basis for characterizing knowledge as inadequate from the data/analyses presented. [Moderate concern] With regard to self-reported practices, the data do not provide insight into why a certain behavior is not practiced (e.g., doctors might know to wear a mask, but none are available); therefore caution should be exercised in asserting that knowledge/training is the only needed solution. References: Cited references are adequate/appropriate.

REVIEWER	Arne von Delft Registrar in Public Health Medicine, School of Public Health and Family Medicine, University of Cape Town, South Africa
REVIEW RETURNED	24-Jul-2018

GENERAL COMMENTS	I. Overall comments: This is an important topic with limited high quality evidence and I would like to thank the authors for conducting this research. English is not a first language in Ethiopia and there are unfortunately a number of grammatical errors, which means the content is not always clear and may have resulted in inadvertent misrepresentation of methods or results. The methodology needs to be explained in greater detail, please, especially the recruitment, questionnaire design and statistical methods. I recommend that the authors consult a specialist statistician to assist them with their analysis and write-up. I would suggest a simpler analysis approach, acknowledging the various data limitations inherent to the topic and methods used. I think the findings are important and the revisions will hopefully result in a publication. II. Specific comments: Page 2: Abstract 17: Participants: No evidence provided in manuscript of random selection - please elaborate on the recruitment or sampling method followed? 24: Results: There are important statistical concerns which need to be addressed as elaborated on later, please? Page 4:

	32-34: There have been a number of studies looking at the prevention of TB transmission (which is not different to the prevention of MDR-TB transmission), esp. in Southern Africa - please consider referencing these and rephrasing. Page 5: 8: Is this date (2014) correct? If so, why did it take four years to submit this paper, or has it been submitted previously to other journals? 17: Please expand on what the high TB detection rate of 34% means - TB detected among which population? 25: Also include more information on Felege Hiwot Referral Hospital as you did with Gondar University Hospital, please? 36: Please add details about the size and staff numbers of the second hospital. 30-38: Please provide more information on how participants were recruited into the study – in the abstract you state they were randomly selected? If so, please provide details? Also related to the response rate on page 6: 33. 41-50: Data collection: Please provide more information about how the questionnaire was developed, structured and pre-tested? Did you adapt any existing tools or questionnaires? If not, please state so clearly and give a brief explanation of the content/questions selected for inclusion, expanding on the last part of the related paragraph. Also add copies of the questionnaire and any related informational, ethics and/or informed consent documents as addenda, please? Did every question have options to select from or were some free text? Page 6: 1: Would rather categorise knowledge as above and below average, since the score is only a reflection of the study sample (internal validity only) if you use the study mean as the cut-off. 1-10: Would list the practice questions in the addendum and supply more information about why these were selected and how responses were assessed (as with the knowledge questions). 13-25: Require more information about the multivariate model selection and testing, please? 44: Did 36.6% of all participants have at least one previous diagnosis of TB? If so, that is an alarmingly high number and worth further focus in the analysis of results and discussion. 50: The mean was used as the cut-off for knowledge scores, yet only 39.5% were above that cut-off? Please clarify? Limit inferences about binary knowledge scores to associations with other factors. Page 7:

	11: Comparing actual scores (rather than a cut-off using the mean) would be more informative for me. You also need to specify which factors were adjusted for, please? 24: How was 'good practice' defined or scored? 36: How did you assess whether variables were independent? Did you try to account for possible clustering at hospital level? 46: 26-30 years was the average age range, not 'older' - reported mean was 27.6. Would rather include age as a continuous variable and interpret accordingly. Page 8: 5: Can't interpret the number of people who scored above or below your knowledge cut-off, given that you used the mean. 46: And did the health workers use the N95 respirators? Question appeared to only deal with access, not self-reported practice? Page 9: 6: Expand on limitations, please? E.g. possible selection bias - the number of health workers who had prior TB appeared to be exceptionally high, suggesting they may have been more interested/willing to participate? 36-48: Informed consent would have been required from the participants in a South African setting. Could the authors please submit a copy of the ethics approval letter from the ERB of the University of Gondar? Page 10: 1: References: Overall the references look adequate, but there are some more recent and/or broad (e.g. systematic reviews) references that could also be considered, especially regarding infection control in healthcare settings. Page 14: As suggested before, less complicated analysis may be more suitable, e.g. overuse of crude and adjusted odds ratios, when simpler descriptive statistics would be easier to interpret. Also beware of or account for unusual phenomena, e.g. directional change after adjustment (Table 3: working site – pediatrics). And check data on Knowledge on MDR – crude OR should be 0.5 for good, not 2 (Table 3).

VERSION 1 – AUTHOR RESPONSE

Reviewers' Comments to Author:
Reviewer: 1
Reviewer Name: RUTH DIVINE AGUSTIN; Institution and Country: University of the Philippines - Manila, Department of Medicine, PHILIPPINES
How the participant were "randomly selected" was not elucidated in Methods sections.
Response: We have included the following paragraph in the method section of the revised version of the manuscript (on page 5 line 28 and page 6 line 1-6) to explain how the study participants were selected: "To select the study participant random sampling technique was used. First, two of the five

referral hospitals in Amhara region were selected randomly (i.e. Gondar University Referral Hospital, and Felege Hiwot Referal Hospital). Then the sample size was proportionally allocated to the two referral hospitals based on their number of health workers. The list of health workers (i.e. sampling frame) was obtained from the human resource of each hospital. Finally, the sample was selected from each hospital by simple random sampling technique."
There was mention of the development of the questionnaire by "a team of health workers" but it was not specified whether or not the research team or an independent group was involved.
Response: The questionnaire for this study was developed by the research team based on the Ethiopia Programmatic Management of Drug-resistant Tuberculosis Guideline 20131, the 2014 WHO Guidelines for the Programmatic Management of Drug-resistant Tuberculosis2, and previous studies3-7. This information is now included in the revised version of the manuscript on page 6 line 9-12.
Specifics on the questionnaire used should be mentioned (e.g. what choices for each question, how the correctness of each answer was determined, how knowledge and practice were categorized as poor or good, etc).
Response: The questionnaire contains the following section: socio-demographic profile of the participants (such as age, sex, marital status, level of education, years of experience, type of occupation); and knowledge and practice of health workers about MDR-TB. Knowledge of health workers was assessed based on the number of correct answers provided to 10 closed-ended questions (i.e. multiple choice, yes/no and true/false) on the definition, cause, diagnosis, treatment and prevention of MDR-TB. Each attracts a score of one (for a correct answer) or zero (for a wrong answer). The knowledge score was calculated for each study participants by summing up the points of all questions, and the score ranging from 0 to 10. Then knowledge score was categorized into good and poor score if it is equal to or above the mean and below the mean respectively. Similarly, the self-reported practice of health workers about MDR-TB prevention and control was assessed by seven questions on access to the MDR-TB guideline, implementation of cross ventilation in the hospital, provision of health education to the patients about MDR-TB, and access and use of Masks N95. If there was a self-reported practice earned a score of one otherwise zero. Participants who scored equal to or above the mean were considered as having a good practice and below the mean considered as a poor practice. This information is now added in the revised version of the manuscript on page 6 line 12-26
In terms of the statistics, it was not explained why a p-value of 0.2 was used.
Response: A bivariate logistic regression model was first fitted, and the variables which had a p-value <0.2 in the bivariate analysis were fitted in the final multivariable logistic regression model. Variables with a p-value <0.05 in the final multivariable logistic regression model were considered significantly associated with the dependent variables (i.e. knowledge and practice). Crude and adjusted odds ratios (OR) with 95% CI were calculated to measure the strength of association between the dependent and independent variables (on page 7 line 7-12)
Reviewer: 2
Reviewer Name: Nebiyu Hiruy; Institution and Country: Management Sciences for Health, Challenge TB project, Ethiopia
Study setting: the author has to explain how he selected the two hospitals out of the total hospitals
Response: During the study period, the region has five referral hospitals, and the study was conducted in two (randomly selected) of these five referral hospitals: Gondar University Hospital and Felege Hiwot Referral Hospital. This information is now included on page 5 line 4-6.
Data collection instrument: Lacks details on the process followed to prepare the data collection tool.
Response: This is an important point that we should explain further. As we have mentioned above, the questionnaire was prepared by the research team for the purpose of this study. The research team developed the questioner by referring to the national and WHO MDR-TB management guidelines 1 8, and by reviewing previous studies3-7 (page 6 line 9-12)
How did the authors ensure validity of the instrument? What actions were taken?

Response: To improve the adequacy, accuracy and appropriateness of the questionnaire content and face validation was performed. Prior to the main survey, the questioner was pre-tested to assess its clarity and suitability to the study participants. The pre-test was undertaken outside the study sites among 20 health workers (i.e. 5% of the sample) (page 6 line 27-30).
I would like to see the data collection tool.
Response: The questionnaire is now available as an additional file in the appendix.
How are the study participants selected? All of the above need to be described.
Response: To select the study participant random sampling technique was used. First, two among the five referral hospitals in Amhara region were selected randomly (i.e. Gondar University Referral Hospital, and Felege Hiwot Referal Hospital). Then the sample size was proportionally allocated to the two referral hospitals based on their number of health workers. The list of health workers (i.e. sampling frame) was obtained from the human resource of each hospital. Finally, the sample was selected from each hospital by simple random sampling technique (page 5 line 27-28 and page 6 line 1-5).
The cut off points for the study outcomes are not outlined. Example: Knowledgeable?
Response: Knowledge of health workers was assessed based on the number of correct answers provided to 10 closed-ended questions (i.e. multiple choice, yes/no and true/false) on the definition, cause, diagnosis, treatment and prevention of MDR-TB. Each attracts a score of one (for a correct answer) or zero (for a wrong answer). The knowledge score was calculated for each study participants by summing up the points of all questions, and the score ranging from 0 to 10. Then knowledge score was categorized into good and poor score if it is equal to or above the mean and below the mean respectively. The mean knowledge score was seven points out of a total possible score of 10 points (page 6 line 15-2, and page 8 line 6-8).
There are some editorial issues: some of them, Page 6, line 1-10 there are editorial issues Page 7, line 25 editorial issue…participants Page 7, line 40 editorial issue…wards. More detailed feedback can be provided based on your response.
Response: We have corrected all those editorial issues in the revised version of the manuscript.
Reviewer: 3
Reviewer Name: Michael E Thompson; Institution and Country: UNC Charlotte, USA
Below is my review of the Knowledge and practice of health workers about control and prevention of multidrug-resistant tuberculosis in referral hospitals, Ethiopia manuscript
The manuscript addresses the increasingly critical issue of nosocomial MDR-TB via a cross-sectional study of provider knowledge and self-reported practice in Ethiopia. The manuscript is of modest interest and importance, documenting that the state of affairs in Ethiopia is comparable to much of the world.
The cross-sectional, nonrandom sampling design limits the analytic value of the sample beyond descriptive statistics. In addition, the document is poorly edited, with omitted and added words and transposed words (e.g., words instead of wards, note instead of not, forth instead of fourth) sprinkled throughout the text and tables. Recommendation: Consistent with my structured review below, my recommendation is REJECT (MAJOR REVISION)
Response: We appreciate the thoughtful review and constructive suggestions. We have provided a point-by-point response for each specific comment below. We have used a random sampling technique to select the hospitals and study participants. However, we accept that the cross-sectional nature of the study design could be one of the limitations of this study. We have now included this limitation in the discussion section of the revised version of the manuscript on page 10 line 28-29: "…given that the study was based on a cross-sectional study design, it is important to acknowledge that a temporal relationship between the explanatory and outcome variable could not be established."
We have corrected all those editorial issues in the revised version of the manuscript.
Title: The title is adequate.
Response: We thank the reviewer for the positive remark
Abstract: [Minor concern] The abstract contains several editorial errors (missing or added words), but otherwise effectively summarizes the manuscript.

Response: The editorial errors are now corrected in the revised version of the manuscript.
Body: [Minor concern] As noted for the Abstract, the body is not tightly edited.
Response: The body of the abstract is now revised.
Introduction: The introduction provides a concise, well-referenced summary regarding MDRTB globally and in Ethiopia.
Response: We thank the reviewer for this positive feedback.
Methods: [Moderate concern] The methods, while rudimentary, are appropriate to establish a working estimate of provider MDR knowledge and practice, but the convenience sample, as tersely described, unduly limits confidence in the representativeness of the findings. Furthermore, the rigor/validity of the knowledge assessment instrument is not well developed, nor is a rationale for using a relativistic measure (the mean) rather than an objective threshold score to determine "good knowledge," especially as the results presentation (P7 lines 1-5) implies knowledge of some items was deemed more important than other items.
Response: There was no a standard tool to measure the knowledge and practice of health workers towards MDR-TB control and prevention. The questionnaire for this study was therefore developed by the research team based on the Ethiopia Programmatic Management of Drug-resistant Tuberculosis Guideline 201327, and the 2014 WHO Guidelines for the Programmatic Management of Drug-resistant Tuberculosis28. Thus, we preferred to report a mean score value than an objective threshold score to determine "good or poor" knowledge and practice. Thus, we acknowledged that the findings of this study could not be generalized to the country (i.e. Ethiopia). However, the findings of this study could be a representative of health workers in the study area (i.e. Amhara region referral hospitals). Knowledge of health workers was assessed based on the number of correct answers provided to 10 closed-ended questions on the definition, cause, diagnosis, treatment and prevention of MDR-TB. Each attracts a score of one (for a correct answer) or zero (for a wrong answer). The knowledge score was calculated for each study participants by summing up the points of all questions, and the score ranging from 0 to 10. Then knowledge score was categorized into good and poor score if it is equal to or above the mean and below the mean respectively.
Results: [Major concern] The socio-demographic profile lacks benchmarking between the respondents and the overall provider population. Furthermore, the referenced Table 1 (P6, line 44) does not contain the information expected (a missing table?). The body of the manuscript and/or the Table 1 referred to on P7 would benefit from indicating the average total number of correct items to provide a referent for where the poor/good knowledge distinction was made. That information is not evident from the solely item-level presentation.
Response: We accepted this comment and the socio-demographic profile of the respondents is now included separately in Table 1. The number and percent of the correct response to the knowledge questions among health workers are also presented in Table 2.
[Moderate concern] The reasoning for presenting AOR only for education (and which variables were adjusted for) in Table 2 is unclear given the limited description in the methods section.
Response: In the bivariate analysis, sex, working sit, profession, educational status, staff categories, previous history of TB, and taking infection prevention training were significantly associated with knowledge of respondents about MDR-TB. However, in the stepwise multivariate analysis, educational level, previous history of TB, and taking infection prevention training were remained significantly associated with knowledge of respondents about MDR-TB after controlling other factors. This information is now included in the result sections of the manuscript on page 8 line 16-20. The multivariate analysis was adjusted for all variables available in table 3.
[Moderate concern] The language used in describing self-reported practices makes it sound like it has accurately captured actual practice.
Response: We have accepted this comment and self-reported practice is used in the revised version of the manuscript.
[Major concern] Good practice is never defined and items responses not reported, limiting the value of this passage.

Response: Thanks for the insightful comment. The definition of good and poor practice is now included in the updated version of the manuscript: "…self-reported practice of health workers about MDR-TB prevention and control was assessed by seven questions on access to MDR-TB guideline, implementation of cross ventilation in the hospital, provision of health education to the patients about MDR-TB, and access and use of Masks N95. If there was a self-reported practice earned a score of one otherwise zero. Participants who scored equal to or above the mean were considered as having a good practice and below the mean considered as a poor practice (page 6; line 21-26). The mean self-reported practice score was four points out of a total possible score of seven points (Page 9 line 6-8)." The questionnaire used to measure self-reported practice is now included in the appendix as an additional file.

Discussion: The discussion, though limited by the weaknesses in the underlying analysis, is adequate.

Response: We thank the reviewer for this positive remark.

Conclusions: [Major concern] Since poor knowledge was defined relativistically (being below the mean), the authors have no basis for characterizing knowledge as inadequate from the data/analyses presented.

Response: As suggested by the reviewer, we have modified our conclusions in the revised version of the manuscript (page 2 line 26-28 and page 11 line 2-6). The definition of knowledge is now clearly mentioned in the method and result section of the revised manuscript.

[Moderate concern] With regard to self-reported practices, the data do not provide insight into why a certain behavior is not practiced (e.g., doctors might know to wear a mask, but none are available); therefore caution should be exercised in asserting that knowledge/training is the only needed solution.

Response: The conclusion is now revised to address this concern.

References: Cited references are adequate/appropriate.

Response: We thank the reviewer for this positive feedback.

Reviewer: 4

Reviewer Name: Arne von Delft; Institution and Country: Registrar in Public Health Medicine, School of Public Health and Family Medicine, University of Cape Town, South Africa

Overall comments:

This is an important topic with limited high quality evidence and I would like to thank the authors for conducting this research. English is not a first language in Ethiopia and there are unfortunately a number of grammatical errors, which means the content is not always clear and may have resulted in inadvertent misrepresentation of methods or results.

The methodology needs to be explained in greater detail, please, especially the recruitment, questionnaire design and statistical methods. I recommend that the authors consult a specialist statistician to assist them with their analysis and write-up. I would suggest a simpler analysis approach, acknowledging the various data limitations inherent to the topic and methods used. I think the findings are important and the revisions will hopefully result in a publication.

Response: We greatly appreciate the reviewer's efforts to carefully review the paper and provide important comments and positive remarks. We have incorporated the suggestions into the revised version of the manuscript

II. Specific comments:

Page 2:

Abstract

17: Participants: No evidence provided in manuscript of random selection - please elaborate on the recruitment or sampling method followed?

Response: We thank the reviewer for this important feedback, and fully agree that further elaboration regarding random selection would be quite valuable. Unfortunately, we needed to reduce the word count in the abstract to fall within the required length, and thus providing more detail around sample selection would not be feasible. However, detail sampling procedure is now included in the method sections of the revised version of the manuscript (page 5 line 27-28 and page 6 line 1-5).

24: Results: There are important statistical concerns which need to be addressed as elaborated on later, please?
Response: The statistical concerns have been revised in the new version of the manuscript and all the necessary corrections have been made.
Page 4:
32-34: There have been a number of studies looking at the prevention of TB transmission (which is not different to the prevention of MDR-TB transmission), esp. in Southern Africa - please consider referencing these and rephrasing.
Response: Additional and more recent studies have been included in the revised version of the manuscript. In the introduction section on page 4 line 16-19, we have included that “Health workers have the potential to contact with MDR-TB patients, and are very important stakeholders in health care settings to combat MDR-TB. Previous studies have been conducted to assess the knowledge and practices of health workers towards the prevention and control of TB9-13.”
Page 5:
8: Is this date (2014) correct? If so, why did it take four years to submit this paper, or has it been submitted previously to other journals?
Response: The manuscript has been previously submitted to another journal and that takes unfortunately a long time.
17: Please expand on what the high TB detection rate of 34% means - TB detected among which population?
Response: This comment is also important. We have now incorporated a definition for TB detection in the method sections of the revised manuscript on page 5 line 8-11, as “TB case detection rate (all forms), which is defined as the number of new and relapse TB cases notified in a given year, divided by the estimated number of incident TB cases for the same year, is 34% in Amhara region.”
25: Also include more information on Felege Hiwot Referral Hospital as you did with Gondar University Hospital, please? 36: Please add details about the size and staff numbers of the second hospital.
Response: These are also important comments. We have now included additional information about Felege Hiwot Referral Hospitals in the method section of the paper (page 5; lines 17-21): “Felege Hiwot Referral Hospital is located in Bahirdar (the capital city of Amhara National Regional State), 562 km northwest of Addis Ababa and 180 km southeast Gondar. The hospital serves a catchment population of more than five million, and about 500 clients visit the hospital daily. It has 273 beds offering different specialized services in four major departments: the Pediatrics, Surgery, Gynecology and Obstetrics and Internal Medicine. ”
30-38: Please provide more information on how participants were recruited into the study – in the abstract you state they were randomly selected? If so, please provide details? Also related to the response rate on page 6: 33.
Response: Detail information about sampling procedure is now included in the method section of the updated version of the manuscript on page 5 line 27-28, and page 6 line 1-5: “To select the study participant random sampling technique was used. First, two of the five referral hospitals in Amhara region were selected randomly (i.e. Gondar University Referral Hospital, and Felege Hiwot Referal Hospital). Then the sample size was proportionally allocated to these hospitals based on their number of health workers. The list of health workers (i.e. sampling frame) was obtained from the office of human resource of each hospital. Finally, the sample was selected from each hospitals by simple random sampling technique.” A total of 377 health workers participated in the study, with a response rate of 93.7% (on page 7 line 24).
41-50: Data collection: Please provide more information about how the questionnaire was developed, structured and pre-tested? Did you adapt any existing tools or questionnaires? If not, please state so clearly and give a brief explanation of the content/questions selected for inclusion, expanding on the last part of the related paragraph.
Response: We have included the following paragraph in the introduction section of the revised version of the manuscript (on page 6, line 12-26 and line 27-29) to explain more how the questionnaire was

developed: “The questionnaire contains the following section: socio-demographic profile of the participants (such as age, sex, marital status, level of education, years of experience, type of occupation); and knowledge and practice of health workers about MDR-TB. Knowledge of health workers was assessed based on the number of correct answers provided to 10 closed-ended questions (i.e. multiple choice, yes/no and true/false) on the definition, cause, diagnosis, treatment and prevention of MDR-TB. Each attracts a score of one (for a correct answer) or zero (for a wrong answer). The knowledge score was calculated for each study participants by summing up the points of all questions, and the score ranging from 0 to 10. Then knowledge score was categorized into good and poor score if it is equal to or above the mean and below the mean respectively. Similarly, the self-reported practice of health workers about MDR-TB prevention and control was assessed by seven questions on access to the MDR-TB guideline, implementation of cross ventilation in the hospital, provision of health education to the patients about MDR-TB, and access and use of Masks N95. If there was a self-reported practice earned a score of one otherwise zero. Participants who scored equal to or above the mean were considered as having a good practice and below the mean considered as a poor practice. To improve the adequacy, accuracy and appropriateness of the questionnaire content and face validation was performed. Prior to the main survey, the questioner was pre-tested among 20 health workers (i.e. 5% of the sample) in other hospitals.”
Also add copies of the questionnaire and any related informational, ethics and/or informed consent documents as addenda, please?
Response: The questionnaire (with informed consent) and ethics approval letter are now available as additional files in the appendix.
Did every question have options to select from or were some free text?
Response: As we have already described, the knowledge questions have closed-ended questions (with one correct answers) that contain multiple choice, yes/no and true/false options.
Page 6:
1: Would rather categorise knowledge as above and below average, since the score is only a reflection of the study sample (internal validity only) if you use the study mean as the cut-off.
Response: The mean score value was seven for knowledge and four for self-reported practice and the results have not been changed when we categorised knowledge and practice as above and below average.
1-10: Would list the practice questions in the addendum and supply more information about why these were selected and how responses were assessed (as with the knowledge questions).
Response: We have accepted this comment and revised the paragraph as follow (on page 6 line 21-26): “Similarly, practice of health workers about MDR-TB prevention and control was assessed by seven questions focusing on access to MDR-TB guideline, implementation of cross ventilation in the hospitals, provision of health education to the patients about MDR-TB, and use of Masks N95. If there was self-reported practice earned a score of 1 if not score 0. Participants who score equal to or above the mean are considered had a good practice and below the mean had poor practice.” The questions used to measure the self-reported practice are now available in the appendix.
13-25:Require more information about the multivariate model selection and testing, please?
Response: This is also an important point that we should explain further. A bivariate logistic regression model was first fitted, and the variables which had a p-value <0.2 in the bivariate analysis were fitted in the final multivariable logistic regression model. Variables with a p-value <0.05 in the final multivariable logistic regression model were considered significantly associated with the dependent variables (i.e. knowledge and practice). Crude and adjusted odds ratios (OR) with 95% CI were calculated to measure the strength of association between the dependent and independent variables. We have included this information in the updated version of the manuscript page 7 line 7-12.
44: Did 36.6% of all participants have at least one previous diagnosis of TB? If so, that is an alarmingly high number and worth further focus in the analysis of results and discussion.

Response: Yes, 36.6% of all participants have at least one previous diagnosis of TB. We agree that this is an important area that requires further analysis and study. However, this is out of the scope of the current study.
50: The mean was used as the cut-off for knowledge scores, yet only 39.5% were above that cut-off? Please clarify? Limit inferences about binary knowledge scores to associations with other factors.
Response: The mean knowledge score was seven points out of a total possible score of 10 points. Two-fifth (39.5%) (95% CI: 35.0%, 44.3%) of respondents scored equal to or more than the mean score which was categorized as good knowledge (on page 8 line 6-8).
Page 7:
11: Comparing actual scores (rather than a cut-off using the mean) would be more informative for me. You also need to specify which factors were adjusted for, please?
Response: The multivariate analysis was adjusted for all variables available in table 3. These includes sex, working sit, profession, educational status, staff categories, previous history of TB, and taking infection prevention training, age, marital status, and working experiences. Since the knowledge score was small (ranging from zero to ten), we preferred to dichotomize the score (based on the average value) and present in odds ratio rather than comparing the actual mean score.
24: How was 'good practice' defined or scored?
Response: To answer this question we have included the following additional information in the revised version of the manuscript (in page 9 line 6-9): "The mean self-reported practice score was four points out of a total possible score of seven points. Less than a quarter (19.6%; 95% CI: 16.2, 23.8%) of health workers were scored equal to or above the mean score which was categorized as good practice towards the prevention and control of MDR-TB. "
36: How did you assess whether variables were independent? Did you try to account for possible clustering at hospital level?
Response: All significant variables were tested for multicollinearity using the variance inflation factor (VIF). This sentence is now revised (page 9 line 13-14).
46: 26-30 years was the average age range, not 'older' - reported mean was 27.6. Would rather include age as a continuous variable and interpret accordingly.
Response: This comment is well considered and the interpretation of age has been corrected in the updated version of the manuscript (on page 9 lines 16-19).
Page 8:
5: Can't interpret the number of people who scored above or below your knowledge cut-off, given that you used the mean.
Response: This is corrected in the updated version of the manuscript (page 9 line 23).
46: And did the health workers use the N95 respirators? Question appeared to only deal with access, not self-reported practice?
Response: There was also a question about "how often do you use them (N95)?" to measure self-reported practice. However, the sentence in the discretion section is now corrected (page 10 line 15-17).
Page 9:
6: Expand on limitations, please? E.g. possible selection bias - the number of health workers who had prior TB appeared to be exceptionally high, suggesting they may have been more interested/willing to participate?
Response: We have accepted this comment and expanded the limitation of our study in the revised version of the manuscript on page 10 line 22-29 as "This study has several limitations. First, there is a possibility that health workers may not report their actual practices (due to social desirability bias) as the information was self-reported. Second, the findings of this study may not be generalizable to health workers in other hospitals of the country as the study was limited only to two referral hospitals in Amhara region. Third, there could be a possibility of selection bias as the number of health workers who had prior TB appeared to be exceptionally high (36.6%), suggesting they may have been more interested to participate in the study. Fourth, given that the study was based on a cross-sectional

study design, it is important to acknowledge that a temporal relationship between the explanatory and outcome variable could not be established."
36-48: Informed consent would have been required from the participants in a South African setting. Could the authors please submit a copy of the ethics approval letter from the ERB of the University of Gondar?
Response: A scanned copy of the ethics approval letter from the ERB of the University of Gondar is now available in the appendix.
Page 10:
1: References: Overall the references look adequate, but there are some more recent and/or broad (e.g. systematic reviews) references that could also be considered, especially regarding infection control in healthcare settings.
Response: We have now included recent references in the revised version of the manuscript.
Page 14:
As suggested before, less complicated analysis may be more suitable, e.g. overuse of crude and adjusted odds ratios, when simpler descriptive statistics would be easier to interpret. Also beware of or account for unusual phenomena, e.g. directional change after adjustment (Table 3: working site – pediatrics).
Response: In the revised version of the manuscript we have tried to use both descriptive analytical statistics for the result and discussion sections. Given that the study was based on a cross-sectional study design, it is important to acknowledge that a temporal relationship between the explanatory and outcome variable could not be established. This limitation has been included in the revised version of the manuscript.
And check data on Knowledge on MDR – crude OR should be 0.5 for good, not 2 (Table 3).
Response: This is also now corrected in the updated version of the manuscript
References
1. Biruck Kebede BA, Anteneh Kassa, Wubaye Walelgne, Andargachew Kumsa, Addisalem Yilma, Lelisa Fekadu, Birru Shigut, Kasech Sintayehu, Solomon Hassen, Etsegenet, Endale Mengesha, Abebaw Kebede. Guidelines on Programmatic Management of Drug Resistant Tuberculosis in Ethiopia. In: Health FDROEMO, ed. Addis Ababa, Ethiopia 2013.
2. WHO. Companion handbook to the WHO guidelines for the programmatic management of drug-resistant tuberculosis. Geneva, Switzerland, 2014.
3. Hashim D, Al Kubaisy W, Al Dulayme A. Knowledge, attitudes and practices survey among health care workers and tuberculosis patients in Iraq. 2003.
4. Hoa NP, Chuc NTK, Thorson A. Knowledge, attitudes, and practices about tuberculosis and choice of communication channels in a rural community in Vietnam. Health Policy 2009;90(1):8-12.
5. Kiefer EM, Shao T, Carrasquillo O, et al. Knowledge and attitudes of tuberculosis management in San Juan de Lurigancho district of Lima, Peru. The Journal of Infection in Developing Countries 2009;3(10):783-88.
6. Kanjee Z, Catterick K, Moll A, et al. Tuberculosis infection control in rural South Africa: survey of knowledge, attitude and practice in hospital staff. Journal of Hospital Infection 2011;79(4):333-38.
7. van der Werf MJ, Langendam MW, Huitric E, et al. Knowledge of tuberculosis treatment prescription of health workers: A systematic review. European Respiratory Journal 2011:erj01256-2011.
8. WHO. Companion handbook to the WHO guidelines for the programmatic management of drug-resistant tuberculosis. Geneva, Switzerland World Health Organization, 2014.
9. van der Westhuizen H-M, Kotze K, Narotam H, et al. Knowledge, attitudes and practices regarding TB infection control among health science students in a TB-endemic setting. International Journal of Infection Control 2015;11(4).
10. von Delft A, Dramowski A, Sifumba Z, et al. Exposed, but not protected: More is needed to prevent drug-resistant tuberculosis in healthcare workers and students. Clinical Infectious Diseases 2016;62(suppl_3):S275-S80.

11. Nathavitharana RR, Peters J, Lederer P, et al. Engaging health-care workers to reduce tuberculosis transmission. The Lancet infectious diseases 2016;16(8):883-85.
12. Nathavitharana RR, Bond P, Dramowski A, et al. Agents of change: the role of healthcare workers in the prevention of nosocomial and occupational tuberculosis. La Presse Médicale 2017;46(2):e53-e62.
13. Gizaw GD, Alemu ZA, Kibret KT. Assessment of knowledge and practice of health workers towards tuberculosis infection control and associated factors in public health facilities of Addis Ababa, Ethiopia: A cross-sectional study. Archives of public health 2015;73(1):15.