

## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Global prevalence of diabetes mellitus in patients with tuberculosis: a systematic review and meta-analysis protocol
<b>AUTHORS</b>	Tankeu, Aurel; Bigna, Jean Joel; Nansseu, Jobert Richie; Endomba, Francky Teddy; Wafeu, Guy; Kaze, Arnaud; Noubiap, Jean Jacques

### VERSION 1 - REVIEW

<b>REVIEWER</b>	João Cordeiro da Costa Pulmonology Service, Centro Hospitalar de Leiria, Leiria, Portugal EPIUnit - Public Health Institute, University of Oporto, Oporto, Portugal.
<b>REVIEW RETURNED</b>	10-Dec-2016

<b>GENERAL COMMENTS</b>	<p>Greetings Dr. Jean Jacques Noubiap and colleagues:</p> <p>Congratulations for your protocol and for your idea. The relationship between Tuberculosis (TB) and Diabetes mellitus (DM) is an important issue and a matter of debate worldwide. There are several studies from different regions that appoint to very discrepant co-prevalence. A major issue is to understand the still unknown physiopathology of the interaction between TB and DM. In general your protocol is well designed, with a clear research question and a quality research plan. However there are several issues that, in my opinion, need some improvement/clarification.</p> <p>1. Inclusion Criteria (Lines 34-49): You include "extra-pulmonary" TB. The pulmonary TB diagnosis is very clear. However extra-pulmonary TB has not a so clear diagnosis pipeline: for instance, in some cases it is a presumption diagnosis based on histology without culture of <i>Mycobacterium tuberculosis</i>. How will you lead with these uncertain diagnoses? Since they are non-contagious it is worthwhile to have extra-pulmonary TB in the analysis?</p> <p>2. Inclusion criteria (Line 48): You miss the last reference "WHO criteria []".</p> <p>3. Exclusion criteria (bullet 1): Why will you exclude letters? For instance with this exclusion criterion you will miss one of the largest European studies (Reference "Cordeiro da Costa J, Oliveira O, Baía L, Gaio R, Correia-Neves M, Duarte R. Prevalence and factors associated with diabetes mellitus among tuberculosis patients: a nationwide cohort. <i>Eur Respir J.</i> May 2016;13993003.00254-2016-. doi:10.1183/13993003.00254-2016."). It would be worthwhile to include all major publication types.</p> <p>4. Exclusion criteria (Line 15): "Studies where the diagnosis of DM is</p>
-------------------------	---

	<p>not based on standard and validated criteria.” You will include patients with “self-report” DM diagnosis (inclusion criteria, line 47). Since even self-report is considered it seems to me that this exclusion criterion is unnecessary since it is unfeasible to evaluate.</p> <p>5. Bibliographic database searches (point A): You state that you will search “online journals”. It would be worthwhile to state what journals and the selection criteria.</p> <p>6. Bibliographic database searches: You state in the abstract “Relevant abstracts in English/French”; first the abstract can’t have information unavailable in the full text protocol; second you may miss many important studies in other languages (Spanish, Chinese, Japanese, Portuguese...). If you decide to include only English/French languages publications you need to state it in the limitations since it is a source of bias.</p> <p>7. Bibliographic database searches: You state in the abstract “unpublished papers and conference proceedings will be checked”; again the abstract can’t have information unavailable in the full text protocol; second it would be worthwhile to state what conferences and the reasons for their selection (this kind of study should be reproducible).</p> <p>8. Selection of studies deemed relevant for inclusion in the review: Who is the “third reviewer” for arbitration?</p> <p>9. Table 1 (query): You should include the most exhaustive query possible. You may not miss terms like “pleurisy” or “diabetic*<sup>o</sup>”. You need to state if you will only search “Mesh Major topics”, “Mesh terms” or for instance “Title/abstract” (PubMed).</p>
--	--

<b>REVIEWER</b>	Yan Lin International Union Against Tuberculosis and Lung Disease, China
<b>REVIEW RETURNED</b>	12-Jan-2017

<b>GENERAL COMMENTS</b>	<p>This is a very useful review of current data from available studies, and helps focus attention on prevalence of diabetes in TB patients. The design and objective is clear with detailed inclusion and exclusion criteria. No major comment, but just a few minor suggestions:</p> <p>1. The conclusion is superficial, and it would have been very helpful if providing a range of prevalence; or different prevalence in particular settings.</p> <p>2. It would be even better if pointing out future study need in understanding prevalence of diabetes in TB patients.</p>
-------------------------	--

### VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: João Cordeiro da Costa

Institution and Country: Pulmonology Service, Centro Hospitalar de Leiria, Leiria, Portugal, EPIUnit - Public Health Institute, University of Oporto, Oporto, Portugal

R1: Greetings Dr. Jean Jacques Noubiap and colleagues:

Congratulations for your protocol and for your idea. The relationship between Tuberculosis (TB) and Diabetes mellitus (DM) is an important issue and a matter of debate worldwide. There are several studies from different regions that appoint to very discrepant co-prevalence. A major issue is to understand the still unknown physiopathology of the interaction between TB and DM. In general your protocol is well designed, with a clear research question and a quality research plan. However there are several issues that, in my opinion, need some improvement/clarification.

Authors: We are most grateful to the reviewer for this appreciation. We also thank you for all the comments and suggestions made, which have undoubtedly and substantially increased the quality and clarity of the manuscript.

R1: 1. 1. Inclusion Criteria (Lines 34-49): You include “extra-pulmonary” TB. The pulmonary TB diagnosis is very clear. However extra-pulmonary TB has not a so clear diagnosis pipeline: for instance, in some cases it is a presumption diagnosis based on histology without culture of *Mycobacterium tuberculosis*. How will you lead with these uncertain diagnoses? Since they are non-contagious it is worthwhile to have extra-pulmonary TB in the analysis?

Authors: Thank you dear reviewer for pointing out this issue. We will consider extra-pulmonary tuberculosis diagnosed by culture of *Mycobacterium tuberculosis* and also those which will have been treated as such despite the absence of culture of *Mycobacterium Tuberculosis*. However, this second group will not be considered for the meta-analysis but will be used for the narrative part review.

R1: 2. Inclusion criteria (Line 48): You miss the last reference “WHO criteria [ ]”

Authors: Thank you dear reviewer for this important remark. The corresponding reference have been added

R1: 3. Exclusion criteria (bullet 1): Why will you exclude letters? For instance with this exclusion criterion you will miss one of the largest European studies (Reference “Cordeiro da Costa J, Oliveira O, Baía L, Gaio R, Correia-Neves M, Duarte R. Prevalence and factors associated with diabetes mellitus among tuberculosis patients: a nationwide cohort. *Eur Respir J.* May 2016;13993003.00254-2016-. doi:10.1183/13993003.00254-2016.”). It would be worthwhile to include all major publication types.

Authors: Thank you for this interesting suggestion. Accordingly, we have removed this exclusion criterion in order to include such relevant studies

R1: 4. Exclusion criteria (Line 15): “Studies where the diagnosis of DM is not based on standard and validated criteria.” You will include patients with “self-report” DM diagnosis (inclusion criteria, line 47). Since even self-report is considered it seems to me that this exclusion criterion is unnecessary since it is unfeasible to evaluate.

Authors: Thank you for raising this discrepancy. This exclusion criterion has been removed.

R1.5. Bibliographic database searches (point A): You state that you will search “online journals”. It would be worthwhile to state what journals and the selection criteria. Pg 10 line 57, {citation}.

Authors: : Thank you Dear Reviewer for highlighting this concern. A word was omitted and has thus been added. The sentence now reads as follow “Relevant abstracts on the prevalence of DM among TB patients will be identified via searching PubMed, Excerpta Medica Database (Embase), Index Medicus and African online journals.”

R1: 6. Bibliographic database searches: You state in the abstract “Relevant abstracts in English/French”; first the abstract can’t have information unavailable in the full text protocol; second you may miss many important studies in other languages (Spanish, Chinese, Japanese, Portuguese...). If you decide to include only English/French languages publications you need to state

it in the limitations since it is a source of bias.

Authors: Thank you dear reviewer for this suggestion. But since most of paper now are published in English even from researchers in countries where English is not the official language, most of the studies on the topic are expected to be in English. But we acknowledged that this is a limitation of our review.

R1: 7. Bibliographic database searches: You state in the abstract “unpublished papers and conference proceedings will be checked”; again the abstract can’t have information unavailable in the full text protocol; second it would be worthwhile to state what conferences and the reasons for their selection (this kind of study should be reproducible).

Authors: Thank you for the suggestion, considering your comments and the limits of such studies; we have finally excluded this inclusion criterion.

R1.8. Selection of studies deemed relevant for inclusion in the review: Who is the “third reviewer” for arbitration?

Authors: The third reviewer will be a member of the review team (JJNN). In addition, we added the names of the two reviewers in charge of selection and inclusion of eligible articles.

R1. 9. Table 1 (query): You should include the most exhaustive query possible. You may not miss terms like “pleurisy” or “diabetic\*”. You need to state if you will only search “Mesh Major topics”, “Mesh terms” or for instance “Title/abstract” (PubMed).

Authors: Thank you for your suggestion. The search strategy has been corrected accordingly.

Reviewer: 2

Reviewer Name: Yan Lin

Institution and Country: International Union Against Tuberculosis and Lung Disease, China

This is a very useful review of current data from available studies, and helps focus attention on prevalence of diabetes in TB patients. The design and objective is clear with detailed inclusion and exclusion criteria. No major comment, but just a few minor suggestions.

Authors: We are most grateful to you for this appreciation. We also thank you for all the comments and suggestions made, which have undoubtedly and substantially increased the quality and clarity of the manuscript.

The manuscript might be improved by carefully considering the following points:

R2: 1.The conclusion is superficial, and it would have been very helpful if providing a range of prevalence; or different prevalence in particular settings.

Authors: Dear reviewer, thank you for this comment. Reviewer should note that this is protocol. We think that the protocol does not need any information on prevalence. This protocol is to describe what we will do and how to have the accurate prevalence of diabetes mellitus among TB patients.

Information on prevalence will be largely discussed in the final report of the project. However, we improved the conclusion by adding some suggestions that made.

R2: 2. It would be even better if pointing out future study need in understanding prevalence of diabetes in TB patients.

Authors: Thank you for this suggestion. We have added the suggestion point as follows: “Much more, this review may identify the research gaps and remaining challenges that may form the basis of future studies to improve our understanding of the prevalence and impact of DM in TB patients.”

## VERSION 2 – REVIEW

<b>REVIEWER</b>	João Cordeiro da Costa Pulmonology Service, Centro Hospitalar de Leiria, Leiria, Portugal EPIUnit - Public Health Institute, University of Oporto, Oporto, Portugal
<b>REVIEW RETURNED</b>	18-Feb-2017

<b>GENERAL COMMENTS</b>	<p>Congratulations for your protocol and for your work of revision. You made substantial improvements and in my opinion it is almost done.</p> <p>There are two minor revisions I encourage you to do:</p> <ol style="list-style-type: none"><li>1. Your reference #12 is stated in the text for both TB and DM diagnosis - perhaps you missed the WHO TB document reference.</li><li>2. The detailed “limitations” point should be in the full text. You can just do a summary in the abstract.</li></ol>
-------------------------	--

<b>REVIEWER</b>	Yan Lin International Union Against Tuberculosis and Lung Disease
<b>REVIEW RETURNED</b>	09-Feb-2017

<b>GENERAL COMMENTS</b>	The authors have incorporated all comments and suggestions made by the reviewers. I have no further comment and fully agree to publish this paper.
-------------------------	--

## VERSION 2 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: João Cordeiro da Costa

Institution and Country: Pulmonology Service, Centro Hospitalar de Leiria, Leiria, Portugal, EPIUnit - Public Health Institute, University of Oporto, Oporto, Portugal

Please state any competing interests: None declared

Dear authors:

Congratulations for your protocol and for your work of revision. You made substantial improvements and in my opinion it is almost done.

There are two minor revisions I encourage you to do:

Authors: Thank you dear reviewer for this appreciation and for all the comments and suggestions made, which have substantially increased the quality and clarity of the manuscript. Thus, we welcome all new suggestion

R1)1. Your reference #12 is stated in the text for both TB and DM diagnosis - perhaps you missed the WHO TB document reference.

Authors: Thank you dear reviewer for this remark. Indeed, we had missed the reference on the diagnosis of tuberculosis. This has been added in the text.

R1) 2. The detailed “limitations” point should be in the full text. You can just do a summary in the

abstract.

Authors: Thank you dear reviewer for this suggestion. The manuscript has been modified accordingly.

Responses to reviewer n2

Reviewer: 2

Reviewer Name: Yan Lin

Institution and Country: International Union Against Tuberculosis and Lung Disease

Please state any competing interests: None declared

Please leave your comments for the authors below

The authors have incorporated all comments and suggestions made by the reviewers. I have no further comment and fully agree to publish this paper.

Authors: We thank you for all your invaluable comments and corrections that have enabled us to improve our manuscript. We are most grateful for your time and your expertise that you have kindly shared with us.