Author’s response to reviews

Title: Co-morbidities of mental disorders and chronic physical diseases in developing and emerging countries: a meta-analysis

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Author’s response to reviews:

Limoges, October 27th, 2018
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To the attention of
Mrs Eva Szunyogova
BMC Public Health
Dear Editor,
Thank you very much for the opportunity to submit a revised version of our Manuscript ID PUBH-D-18-01218 entitled «Meta-analysis of comorbidities of mental disorders in developing and emerging countries."

We thank the reviewers for their valuable comments - they helped us to clarify our paper, and we have addressed the issues point by point.

We attach a version of our revised paper without “track changes” and a second version using the “track changes” option in supplementary material.

We thank you very much and look forward to hearing from you.

Sincerely,

Labanté Outcha Daré, MSc; Pierre-Emile Bruand, PharmD; Daniel Gérard, MD; Benoît Marin, PhD; Valerie Lameyre, MD; Farid Boumédiène, PhD; Pierre-Marie Preux, PhD.

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REVIEWERS REPORTS:

Kenny S Crump (Reviewer 1):

Comment 1:

Page 10, lines 1-4: Here the relative odds of having depression (or depression and anxiety) in persons with chronic physical diseases is reported. However, the stated goal of the study seems to be the converse of this, i.e., the prevalence or relative odds of chronic disease comorbidities in
persons with mental disorders. These are two different outcomes that sometimes appear to be conflated. Clarification is needed here and throughout the paper.

Response 1:

Thank you for raising this point. The goal of our study was to look at both aspects, to look at these associations from a bidirectional point of view: i.e. chronic physical diseases in people with mental disorders and also mental disorders in people with chronic physical diseases. Similarly for neurotropic parasitic diseases, the objective of our study was to investigate both types of comorbidities as described in the Results section page 9-12:

“Pooled estimates and heterogeneity

Prevalence studies

Prevalence of mental disorders in people with chronic diseases

Prevalence of chronic diseases in people with mental disorders

Case-control studies

Odds ratios of mental disorders in people with chronic diseases

Odds ratio of neurotropic parasitic diseases in people with mental disorders”.

and page 9, line 2-5:

“The purpose of this study was to look at associations bi-directionally: mental disorders in people with chronic physical diseases but also chronic physical diseases in people with mental disorders, similarly mental disorders in people with neurotropic parasitic diseases and neurotropic diseases in people with mental disorders”.

We also reviewed the document and checked for consistency with each type of co-morbidity sought in our study.

Comment 2:

Page 10, lines 1-4: Odds ratios should be interpreted in terms of relative odds rather than risk, here and throughout the paper.
Response 2:

Thank you for your comment. We have adjusted accordingly and have ensured that it is also consistent throughout the document.

Results, page 11, line 24-25.

Comment 3:

Page 6, line 12: Please clarify what is meant by "type of origin disease" and "type of associated diseases."

Response 3:

Thanks for your comment. We have now specified in the document what is meant.

Materials and Methods, page 7, line 21-24.

"type of origin disease (type of diseases having a person before the study) and type of associated diseases (type of diseases investigated through the study)".

Comment 4:

Page 12, lines 44-61: Please indicate what countries or continents are included in the meta-analyses cited.

Response 4:

Thank you for your comment. We have taken it into account and have included these countries in the section:

Discussion, page 14, line 11-16:

"some meta-analyses involving countries such as United States, Finland, Canada, Taiwan, Singapore, United Kingdom, China, India, Spain [127], Danemark [136], United States, Belgium, Norway, South Korea, Taiwan, Canada, Australia, Italy, United Kingdom [137], United States, Malaysia, Australia, Taiwan, United Kingdom [138] and United States, Bahrain,
Puerto Rico, Spain, Japan, Australia, Sweden, Canada, Danemark, Netherlands, Bangladesh, United Kingdom, Taiwan, Norway, Finland [139].

Comment 5:
Consider including a sensitivity analysis that excludes studies with the lowest quality scores.

Response 5:
Thank you for raising this point. We performed the sensitivity analysis taking into account the quality of the studies. You will find the information in the following sections:
Materials and Methods, page 7, line 12.
Results, page 10, line 16-32.

Comment 6:
The figures were difficult to follow because they are not numbered; please make sure that each is clearly indicated at the appropriate place in the text.

Response 6:
Thank you for raising this issue. We have ensured that figures are now numbered and each is now clearly indicated in the appropriate place in the text.
Figures, page 36.

Rahul Shidhaye (Reviewer 2):

Comment 1:
Kindly explain why HIV was not included in infectious diseases. Mental disorders and HIV are very strongly associated.
Response 1:

Thank you for raising this point. Indeed, we have inserted this limit in the discussion part.

Discussion, page 15, line 30-32 and page 16, line 1:

“Mental disorders are also very common during the perinatal period. This is a criterion that could have been included in our inclusion criteria. But the objective of this meta-analysis was oriented towards general results. So this type of specificity has not been considered. Another limitation of this study is that HIV is not included in infectious diseases even though mental disorders and HIV are very strongly associated. Future work will need to specifically address co-morbidities with HIV”.

Comment 2:

Mental disorders are also higher during peri-natal period. It is completely fine to exclude this group, but at least mention in discussion that this is an important co-morbidity.

Response 2:

Thank you for this comment. We have taken your point into account by specifying in our discussion the point you raised.

Discussion, page 15, line 27-30.

“Mental disorders are also very common during the perinatal period. This is a group that could have been added to our inclusion criteria. However as this meta-analysis was oriented towards a broader population, this group was not specifically taken into account”.

Comment 3:

Where there are any community-based studies? It seems that all the studies were in hospital setting. This will have important bearing on the overall findings. Please clarify.
Response 3:

Thank you for your question. There were actually no community studies found that met the inclusion criteria. Indeed, all studies were conducted in a hospital setting, either inpatients or outpatients. We have clarified this in the relevant part.

Discussion, page 13, line 30.

Comment 4:

'Non-hospitalized' patients mean patients attending 'out-patient clinics'? Kindly explain.

Response 4:

By "non-hospitalized" we mean patients who live in community or in other words who attended to the health centre (clinic or hospital) for care but who did not stay in the health care centre for one or more nights. We chose to name them this way as opposed to "hospitalized", that is, patients who were staying in a health care centre.

Materials and Methods, page 6, line 24-28.

Comment 5:

On page 13, line 1-2 mention, 'In addition, our meta-analysis revealed that the increased risk for anxiety and/or depression in people with chronic physical diseases was 540% (95% CI, 1.4 - 27.9)."Please check the figures.

Response 5:

Thank you for highlighting the error, this figure has been corrected. Indeed, there was a mistake. The odds ratio is 3.1.

We have changed this in the manuscript in the following section:

Discussion, page 15, line 7.
Comment 6:

It is unclear how 'religion' will have any impact on prevalence estimates. Is this due to selection bias? If so, please clarify further.

Response 6:

We mentioned religion in our discussion to draw attention to the fact that traditional beliefs have been shown to delay and/or be a barrier to the consultation of healthcare professionals. By this we do not mean to imply any selection bias.

The part in our manuscript that is relevant is as follows:

Discussion, page 14, line 18-24.

" This lack of data in developing and emerging countries may be explained by the lack of medical consultations for people with mental disorders and also by the rather reduced number of health centres which, when they exist, are not accessible [140]. In addition, the influence of religion also has a significant impact on the diagnosis of mental disorders in developing and emerging countries. Often wrongly attributed to a spiritual effect, 80% of people with mental disorders and their families prefer to consult religious leaders or healers or exorcist-priests [141].".

Reviewer 2 (Reviewer 3): PEER REVIEWER COMMENTS:

Comment 1:

The aims of this paper are too vague, ambitious and broad in scope. Therefore, the review included studies which are not really compatible. The pooled estimations, as a result, are misleading.

Response 1:

Thank you for your comment. We feel that the methodology used, the inclusion criteria and selection of the studies, data extraction and evaluation of article quality, as well as the statistical analyses performed were appropriate and rigorous. All studies were evaluated by the Down and Black evaluation grid (see Table 4 and Table 5 in the supplementary material). As a result, only studies that met our inclusion criteria were included in our estimates. The overall scope of our
study could open the field to other researchers to further investigate the types of co-morbidities studied in this meta-analysis. Thus, this study will provide an opportunity for more debate in the research that in turn will hopefully lead to further meta-analysis or research shedding new insights on these associations.