Author’s response to reviews

Title: Psychotropic medication non-adherence and associated factors among adult patients with major psychiatric disorders: a protocol for a systematic review

Authors:
Agumasie Semahegn (asdemisie@st.ug.edu.gh)
Kwasi Torpey (ktorpey@hotmail.com)
Abubakar Manu (abumanu@yahoo.com)
Nega Assefa (negaassefa@yahoo.com)
Gezahegn Tesfaye (gezites@gmail.com)
Augustine Ankomah (aankomah@ug.edu.gh)

Version: 2 Date: 07 Nov 2017

Author’s response to reviews:

Cover Letter

Date: 07/11/2017

To: BMC systematic review Journal

Subject: Submission of revised version manuscript (SYSR-D-17-00186R1)

First of all, we would like to thank both of the reviewers and the editor for the continuous effort you made to review and forward your input into our manuscript. We are glad to inform you that we have made the revision on our manuscript as per the journal guideline and reviewers comments entitled “Psychotropic Medication Non-adherence and associated factors among Adult Patients with Major Psychiatric Disorders: a Protocol for a Systematic Review and Meta-analysis: Agumasie Semahegn*1,2, Kwasi Torpey1, Abubakar Manu1, Nega Assefa2, Gezahegn Tesfaye2, 3, Augustine Ankomah1. We tried to address all the comments and also add some revision by ourselves and arranged our response in track change format (submitted as supplementary) to make more visible. We are so delighted to receive any further comments for the betterment of our manuscript. Do not hesitate to ask us if you have any inquiries!

With Kind Regards!
Point-By-Point Response

Psychotropic Medication Non-adherence and Its Determinants among Adult Patients with Major Psychiatric Disorders: a Protocol for a Systematic Review and Meta-analysis

Agumasie Semahgan, Ph.D. student; Kwasi Torpey; Abubakar Manu; Nega Assefa; Gezahegn Tesfaye; Augustine Ankomah: Systematic Reviews (SYSR-D-17-00186R1)

Reviewer reports:

Reviewer #1: The authors have addressed most of my comments in a satisfactory manner and the manuscript is much improved and clearer. However, several key methodological elements are still missing. While the accuracy of the writing is much improved, several grammar errors remain, most notably lack of agreement between subject and predicate in several places (I indicated a few of these).

Response: Thank you so much!

Abstract:

First sentence: psychiatric disorders "are" a growing public health concern (not "is")

Response: Thank you so much: Addressed!

Background

P.3, Line 16 and line 17: "has" instead of "have"

Response: Thank you so much: Addressed!

P.4, Line 11-12: What is the review report? The authors need to give the reference

P.4, Line 12: "are" instead of "is"

Response: Thank you so much: Addressed!

P.4 Line 21: "optimal" instead of "optimum"

Response: Thank you so much: Addressed!
P.4 Line 25-26: replace concise evidence with "systematic reviews and meta-analyses"

Response: Thank you so much: Addressed!

Method:

P5, L.16: removed "composed" I still do not understand at all how the authors will assess quality. The reference cited is a meta-analysis in depression; how will that be used? The authors need to include an instrument to rate the INDIVIDUAL studies and that needs to have been developed for observational research.

Response: Thank you for the comment and we kindly omitted “composed” and addressed the recommendation

The authors give a tool in Appendix 4 and they refer to it further in the Method. How was that tool constructed? Has it been used before and its properties (reliability, validity) tested? Have the authors created it? The authors should search for an already existent and studied tool for assessing the quality of observational research. There are several such tools: see for instance https://www.ncbi.nlm.nih.gov/pubmed/20728045 (a systematic reviews of such tools). It is very counterproductive for the authors to develop their own tool, combining and adapting others, because then we really do not know what this new instrument measures, it has not been studied independently, some items might be relevant, and others not etc

Response: Thank you for the comment and we are so happy to use the quality assessment tool for systematic strengthening the Reporting of Observational Studies in Epidemiology (STROBE).

P.6, l.28-29: If that is an exclusion criteria it should be moved at the description of eligibility criteria.

Response: we thank you for the comment and address as per the recommendation.

P.6: The authors should just use the PRISMA as reporting tool (and appendix 3 needs to be modified to follow the PRISMA). Adapting various guidelines and combining them is a misleading approach to take. The authors then state they will use the MOOSE guideline, which is a PRISMA proposal extension for observational research. The authors need to clarify, they
cannot simply combine reporting guidelines. In order for the results to be comparable, it need to be clear what reporting guideline they will use.

Response: Thank you for the comment and we would like to use PRISMA-P 2015 reporting guideline.

Also, will the abstracts be kept separated and used separately or combined with the other studies?

Response: We thank you for the comment, regarding to abstract, we thought to include abstract that presented in conference but now we decided to exclude abstract or scanty reports unless we get the full report to minimize misleading. Thank you a lot.

The authors still do not give any information about the effect size (ES) measure. As I said before, the authors need to say what quantitative data will be extracted (e.g., counts, rates, correlation coefficients) and what indicators will be derived from these (odds ratios, risk ratios etc).

Response: Thank you for the comment. We will extract non-adherence counts but not rates, correlations or coefficients. We will extract counts (non-adherence count and total sample size) and then computes the pooled rate.

P.7, line 9-11: this part refers to the search and should be moved there. At this section, the authors should detail (or at least give some examples) of what information they will extract from the papers (e.g., type of sample, setting, conditions, etc). They also need to explain how will they study determinants/predictors (combine them in categories? What categories? What basis will they use for constructing these categories?)

Response: We thank you for the comments. Please look at the sample that we will use to describe studies and extract quantitative data in MS Excel sheet.

Sample Study description and data extraction format for future use

<table>
<thead>
<tr>
<th>Author, country</th>
<th>study aim</th>
<th>Design</th>
<th>Population</th>
<th>Sampling procedure</th>
<th>Sample size</th>
<th>Response</th>
<th>Main findings</th>
<th>Conclusion and recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alene et al., 2012</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Ethiopia (40)

To evaluate adherence and factors of non-adherence Cross-sectional Patients with schizophrenia Purposive

336 87.5% The prevalence of non-adherence was 42.5%. Adherence to the medication is low.

Kenfe T. et al, 2013. Ethiopia (42)

To assess the magnitude and associated factors of non-adherence to medication Cross-sectional psychiatric follow-up patients (>18 years) consecutive sample in November 2011 422 100%
Medication non-adherence was 41.2% 78.2% attributed their non-adherence to forgetting. Irregular follow-up, poor social support and complex drug regimen were independently associated variables with non-adherence. non-adherence among psychiatric patients in Southwest Ethiopia is high and revealed possible associated factors.

MS Excel extraction sample

author, year sample size non-adhered
kenfe T. et al , 2013 422 174
Alene et al. 2012 336 161

Reviewer #2: Thank you for inviting me to review the revised version of this protocol.

The authors have tried to address the comments. However, the revision has made this protocol to be open for more critics. I personally liked the idea of narrowing down the perspective of the previous version of the systematic review protocol to the low and middle-income countries. As there is not so much evidence specifically to low and middle-income countries (LMIC), it would have been an important piece of evidence. The need of the review was well-justified. Changing the scope because of the reviewers' questions was not helpful. Anyway, the authors decided to widen the scope of it. As a systematic review author, it is always helpful to balance the scope of a review and the strength of evidence the systematic reviewers would like to generate. The authors are can decide where to focus.
If the authors decide to continue with the current scope, I suggest working on the following comments.

The introduction section particularly paragraph 1, 2, 3 are repetitive. There is an over the description of the global burden of major psychiatric disorders and its sequel. Synthesizing and summarizing the existing evidence is needed to have a clearer and informative overview of the problem on the global scale. Collect all the statements which talk about the same idea and synthesize their ideas along with their citations. The write up could be improved that way.

• Response: we thank you for the comment and we tried to compile the three paragraphs into two.

Proofreading with native English language speaker is essential for this protocol. In many sections of the protocol, there are outstanding English language issues that should be corrected.

• Response: we thank you for the comment. Proof reading addressed as much as possible.

As this protocol is now having a wider scope than it has from its previous form, it is also important to tailor the introduction. There are still statements in the introduction which talks about the burden of psychiatric disorders in LMIC.

• Response: We kindly omit LMIC issues on the introduction to minimize narrowing down the review, and we would like to maintain with a wider scope because mental health is a global issue and the medication adherence gap is common across the globe and worldwide problem. That is what we want to generate evidence.

In my previous comment, I mentioned about the assessment of publication bias. The authors prefer only funnel plot for publication bias. I suggest considering additional statistical strategies to check publication bias using statistical tests such as Egger test and Begg test.

• Response: Thank you for the comment, we addressed the comment in the manuscript. We thank you a lot!

I checked what the authors wrote in the PROSPERO database "We will check potential publication bias by visual inspection of the funnel plot. Besides, Egger's regression test will be
used to statistically check the asymmetry of the funnel plot. Publication bias will be assumed with a P value of less than 0.10". This was right explanation to assess publication bias

As the protocol is already registered in PROSPERO database, make sure to update the scope of it in the PROSPERO database based on the latest scope of the protocol if the authors would like to continue the protocol on its current scope. In addition, there are other issues requiring an update in the PROSPERO eg AMSTAR needs to be replaced with a relevant quality assessment method

• Response: we thank you for the comment. We missed the PROSPERO Updating and now we updated the PROSPERO. Thank you so much!

The methodological quality assessment tool is not appropriate. The ones cited are systematic reviews on methodological quality assessment tools. Please find a relevant tool and justify your choice. In addition, write the main domains of the quality rating scale in the quality assessment section. On page 6 line 6 to 7, the authors wrote: "The following steps will be used sequentially in order to select quality studies for the systematic review and meta-analysis". Mention the main domains of the quality assessment tool. The authors are not clear with quality assessment of studies. The steps subsequently described are about the study selection process. While those steps are important for study selection, it is not possible to rate the quality of a study using these steps described. Most of the stages of systematic review can be automated using relevant tools such as Rayyan mainly helpful for screening, Covidence helpful for many stages of the review process. For more information to learn about more helpful tools, please consult systematic review toolbox webpages (http://systematicreviewtools.com/).

• Response: thank you for the comment and we highly appreciated the link and utilized very well and we are so happy to use the quality assessment tool for systematic strengthening the Reporting of Observational Studies in Epidemiology (STROBE). But we couldn’t find the "Rayyan" through the link that you provided us.

Thank you so much!