Reviewer's report

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

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Reviewer: Ioana Cristea

Reviewer's report:

Overall, the authors should significantly restrict the focus of their meta-analysis and describe the conditions they are focusing on, the types of drugs and why they were chosen. Psychiatric conditions and drugs have very different effectiveness to adverse effects profiles, assessing non-adherence across them leads to results which are impossible to interpret. A lot of general and vague information is presented, in the detriment of specific information related to the review.

There are numerous wording and grammar errors in the text. The abstract at least should be revised, as it is difficult to understand. I do not understand what determinants the authors are looking for, there can be many factors for medication non-adherence. Specifying Word and Excel will be used is a waste of abstract space, the authors should instead give more data about the actual planned analyses, which they describe very generally. PRISMA is a reporting guidelines, so again stating in the abstract that it was used is superfluous.

Introduction:

The authors dedicate a whole page to arguing that psychiatric disorders are a problem. This is already widely-known and this section is superfluous.

Overall, I did not manage to understand well what the authors want to study. Moreover, non-adherence is a concept that does not have much relevance if it is studied in general. Psychiatric disorders and medications are widely different, adherence to lithium is in no way similar to adherence to anti-depressants. I also don't see the link between non-adherence and increased burden of disease; for many of these conditions, the issue is that treatments are not effective. How would it help to be adherent then? For others, the issue is that there are serious side-effects, and like in all domains of medicine, the patient can hardly be blamed that the balance of side-effects to benefits is tipped toward the first one.

The authors present some adherence rates but there is a wealth of literature here, by disorder and the authors should synthesize this literature and certainly not cite an unpublished dissertation (reference 3). The authors do give some sparse references from various disorders, but once again
non-adherence does not have the same causes and even consequences across psychiatric disorders. Again, the link between medication non-adherence and negative consequences of many psychiatric disorders is far from clear, not similar across disorders and I believe in some cases not even existent.

Search strings

Stating search strings will be created based on the research question (p.8) offers virtually no information. I understand the authors don’t have the search string, but at least some key words can be indicated. What is a sample search string? Are those key words that will be used? If yes, the number of records identified seems enormous. How do the authors plan to handle this? The shorter Pubmed string that identifies 625 records has the problem that the authors use just some synonyms for determinants, I suspect many will be hardly ever uses (associated factors/influencing factors, appearing in this phrasing, or even determinant, which is a very causal term), and others that are not in the search string (prognostic, predictive, correlates) will be widely used. This string is probably going to miss a large number of relevant records.

What will be included as psychiatric disorders and what rule will be used?

Also what do the authors planned to do with the many pooled analyses (more trials combined) or secondary analysis of trials that often look ad adherence?

Screening studies based on whether data for the meta-analysis is included in the abstract is insufficient, this will miss the studies where this data is only reported in the paper.

The AMSTAR is a tool for rating the quality of meta-analyses, how can the authors apply it to their papers?

The definition of outcomes is very general. Studies are likely to have defined adherence in different ways. What definition will the authors use? Whatever the original authors give? The authors then say they will also use other indicators like non-compliance and drop-out, how will they be used? Will they be considered equivalent to non-adherence? If yes, they should also be in the search strategy.

Are the authors interested in testing any moderators? Particularly since they have such a large and poorly defined topic, spanning different disorders and treatments, heterogeneity is bound to be a problem and moderator analysis are one possible way to explore that.
Overall many things in this protocol are very vague. The authors just state they will do everything but give very few specific details. For instance, how will study quality be rated? What items will they focus on? Which scales will be used by type of design? The measure of effect size is not specified. What quantitative data will be extracted from the selected papers and how will they be used?

What will the authors do with overlapping data, for instance when several of included articles will have overlapping samples?

There should also be some quantitative way of assessing publication bias. I also don't understand what it means that publication bias will be anticipated based on p values smaller than 0.10 (p 12, l.20-21).

Also, what does high heterogeneity mean (p.12, l.26-27) exactly? Over what limit will the authors not conduct a meta-analysis.

Only one subgroup analysis is planned? The class of drugs is not even mentioned as a potential moderator, but some drugs have more side-effects and this can lead to non-adherence.

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An article whose findings are important to those with closely related research interests

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