Reviewer’s report

Title: Impact of Drug Burden Index on adverse health outcomes in Irish community-dwelling older people: a cohort study

Version: 1 Date: 05 Feb 2019

Reviewer: Zachary Marcum

Reviewer's report:

This is a longitudinal analysis of an observational cohort study of Irish community-dwelling older adults aiming to validate the DBI by examining the association of DBI score with important health outcomes in older adults. This topic is of great importance to improve medication use and safety in older adults. This manuscript was very well written, organized, and logical in its design and execution. Suggestions below are largely to improve clarity and transparency of the study.

ABSTRACT:

- Conclusions: Can you be more specific about what kind of risk is being predicted? For example, "…screening tool for predicting risk of poor health outcomes in older people…"

BACKGROUND:

- Line 20-21: The parent paper (ref 4) that is referenced does not have the aim of developing a DBI screening tool. The primary outcome of that paper was to investigate the prevalence of exposure to DBI medications and patient factors associated with DBI exposure. As part of that, they defined a consensus list of DBI medicines available in Ireland. Unsure of the word 'screening tool' is appropriate in that sense; as it implies a systematic way or electronic tool, that streamlines the process of determining DBI medicines. A more transparent sentence referring to the subset of the DBI medicine list in the parent paper might be more representative of the analysis conducted.

METHODS:

- Medication exposure: Line 14: Related to comment above. Consider revising the use of the term 'DBI screening tool' throughout the entire manuscript.
- Medication exposure: Line 22: Figure 1 illustrates the two cohorts that were used to investigate the effect of DBI related to a different set of outcomes. Please state the rationale for using different cohorts with different follow up times for clarity.

- To improve ease of readability, it would be helpful to explicitly state which outcomes were assess for each cohort in the text in addition to that which is currently stated in the Figure.

- Outcomes: Falls were measured using self-report. This should be included throughout the manuscript (including the tables and footnotes) when describing falls for transparency and accuracy.

- Statistical analyses: It is mentioned that participants with missing data for any outcome, exposure, or covariate were excluded from analysis, but the extent of missingness is not included in the manuscript. This should be clearly stated in the manuscript. Ideally, the authors would compare those participants who were included/excluded from analysis to determine if there are important differences.

RESULTS:

- The results only include the high DBI exposure vs. none, but do not include the low DBI exposure vs. none. Why are these results not reported in the Results section? They are referenced later in the Discussion.

DISCUSSION:

- "We found that increasing exposure to DBI medications…" Suggest using a different word as "increasing" implies that some sort of intervention was done. Consider "high" exposure.

- Para 2, lines 10-11: the word 'approximately' should be inserted before 'two DBI medications', as the 'minimum dose' differs from one medicine to the other, and it would be incorrect to state that the sum of exposure of any two DBI drugs would be equal to a 1-unit increase in the DBI score.

- Para 2, lines 13-14: Insert an example of a positively worded statement to give context to the nature of the statements included in the CASP QoL measure, since there was no pre-text given prior to that sentence.

- Para 5. Please reference other studies that might have had similar or the same conclusions made.
Limitations: The authors point out that the risk of bias is likely to be minimal from medications being purchased OTC. One additional point that could be considered for inclusion is that this bias is likely non-differential across the exposure groups, which is another reason why it is likely not a major concern.

Limitations: One major limitation that the authors did not mention is their lack of adjusting for severity of co-morbid conditions. This should be included.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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Please indicate the quality of language in the manuscript:

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