Reviewer’s report

Title: Patterns of Antihypertensive and Statin Adherence Prior to Dementia: Findings from the Adult Changes in Thought Study

Version: 1 Date: 01 Nov 2018

Reviewer: Edeltraut Kroger

Reviewer’s report:

Dear authors,

I found the idea of using data on patient adherence to screen for early signs of mild cognitive impairment or undiagnosed major neuro-cognitive disorder a great initiative which may pave the way to including the community pharmacist in a more meaningful way in community based geriatric care of frail seniors. I am also aware of the quality of the data used for this study. Nevertheless, the manuscript is somewhat hard to follow and there are several unanswered questions for me.

1) I am unfamiliar with the group-based trajectory modeling technique and it is therefore hard for me to decide how relevant the results based on this technique are. Given that other readers/clinicians may be in the same situation, I would thus suggest that you do parallel analyses in which you'd measure adherence in a more established manner, let's say by the drug-possession rate, for shorter periods (3 or 6 months), and analyse whether the incidence of non-adherence as DPR (below a threshold of 60, 70 or 80%) is associated with incident diagnosis of MNCD. If results agree between those analytical approaches that would strengthen your argument and ease understanding for readers.

2) I also wonder whether it would be feasible to distinguish between patients having been diagnosed with MCI and those with MNCD, and on top of that, possibly identify different disease stages? One might expect adherence to change throughout disease evolution, with early MCI possibly associated with first adherence problems, maybe getting worse with MNCD incidence, and then possibly getting better because help with medication taking is organized.

3) Hypertension is oftentimes treated with more than one medication which makes adherence more challenging - also given the adverse effects of several antihypertensives. In comparison, statins are "rather easy" to take. Could you take this into account in your models? Or in your discussion, please?

4) Are patients diagnosed with MCI or MNCD present in both the antihypertensive AND the statin analysis? If yes, this means that the disease would have influenced adherence to one medication group (antihypertensives), but not the other. This possibility needs to be discussed.
5) I saw no adjustment in your analyses for polypharmacy or medication complexity. We know that these characteristics of pharmacotherapy influence medication adherence in seniors, particularly in vulnerable seniors (Kröger et al, Improving medication adherence among community-dwelling seniors with cognitive impairment: a systematic review of interventions. Int J Clin Pharm, 2017, Aug;39(4):641-656. doi: 10.1007/s11096-017-0487-6. Epub 2017 May 29.) Could you adjust for these characteristics? If not, this needs to be discussed and might also be related to differences between the two studied groups.

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.

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