Author's response to reviews

Title: Potentially inappropriate Medication Use in Nursing Homes. An observational study using the NORGEP-NH Criteria

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Author’s response to reviews:

Authors’ comment:

Again, we would like to thank you for your time and efforts in reviewing this article. We have done our best to address the reviewer’s comments. See author’s comments underneath each comment below.

Reviewer reports:

Emily Reeve, B.Pharm., Ph.D. (Reviewer 1): The authors have addressed many of my original concerns and I believe that the manuscript is improved. I have a few minor suggestions for final consideration.

Abstract - 'PIMs' abbreviation used without first defining it

- Thank you for pointing out this oversight. It is now corrected, line 30.

psychotropic drugs are introduced in the results section perhaps add mention of them in the aim (when mentioning the NORGEP criteria) or methods

- We have added a sentence about psychotropics under “Aims”. In addition, psychotropics are already mentioned in the Background section (lines 82-85), in the Methods section under Statistics (lines 154-155, lines 166-169). We hope the resulting text is satisfactory.
I would suggest including 95% CIs for all ORs (in abstract and throughout the manuscript) to show the precision (as well as the p value)

- Table 4 represents the results from the regression analyses that included all nursing home residents. In this table is included odds ratios, 95% confidence intervals, and p-values for bivariate and multivariate analyses. We have added information about this in line 205 for clarity, and we have edited the headline to Table 4 to clarify the selected regression model. We have therefore chosen to present those results from Table 4 that are also mentioned in the text with odds ratio and p-values only, for readability purposes. However, in four instances we present results that are not included in Table 4, namely when presenting results from the alternative regression model, addressing residents living in long-term facilities only. In these instances, we have chosen to include odds ratios, 95% CIs, and p-values in the text, for precision. We have edited the text to make it more apparent that these results stem from a different regression model (lines 209 and 215) and that these results are not presented in Table 4 (lines 211, 219). We added 95% C.I. in one instance presenting results from long-term residents only, where it had been omitted (line 217). It is our hope that after these clarifications the text is satisfactory. We expect that the results in Table 4 will become more apparent for the reader in the published version when Table 4 is inserted in the intended position in the article, and that when Table 4 is presented close to the referred results, the adding of 95% C.I. in the text will not be needed. However, if the reviewers/editor still would prefer that 95% C.I.s are added to all results in the text, we will be more than happy to comply with those wishes.

Introduction: 'adverse reactions (ADRs)' - this should be adverse drug reactions (ADRs)

- Thank you for pointing out this omission. It is now corrected.

'The NORGEP-NH criteria have not yet been validated per se' - suggest being more specific with this - have not been externally validated against adverse outcomes or as a beneficial tool for practice (is this is what you mean?)

- After consideration, we have chosen to omit this sentence from our article. Our original intention was to point to the fact that the specificity and sensitivity of the NORGEP-NH have not been validated against a “gold standard” in a thorough validation study, like in Wallerstedt, S. M., B. Belfrage and J. Fastbom (2015). "Association between drug-specific indicators of prescribing quality and quality of drug treatment: a validation study." Pharmacoepidemiol Drug Saf 24(9): 906-914. However, these authors know of only the mentioned validation study of this kind in this field. Brown et al also looked at sensitivity and specificity of the STOPP/START and Beers criteria, but without the “gold standard” reference. (Brown, J. D., L. C. Hutchison, C. Li, J. T. Painter and B. C. Martin (2016). "Predictive Validity of the Beers and Screening Tool of Older Persons' Potentially Inappropriate Prescriptions (STOPP) Criteria to Detect Adverse Drug Events, Hospitalizations, and Emergency Department Visits in the United States." J Am Geriatr Soc 64(1): 22-30.) Thus, overall, most such criteria, including the NORGEP-NH, have not yet been validated in this sense of the word. We realize that in its present form, the addressed sentence could be misleading to most readers, and it was therefore omitted here. (A more
A thorough discussion on the matter of validation of external criteria is presented in the main author’s PhD thesis, recently handed in at the University of Oslo).

Aims - please mention psychotropic drug use here

- This has been added.

Methods - just to clarify, were all residents who were hospitalized excluded from this study?

No, most hospitalized patients were included in the study. The aim of the original study was to study differences in outcomes between those treated with intravenous fluids/antibiotics in the nursing homes, after introducing this line of treatment there, and those treated in the local hospital after being admitted there. Since the study was following a stepped-wedge design, patients had to be treated in the hospital before the intervention that consisted in teaching the personnel in the nursing home about intravenous treatments. After the intervention, the patients were treated in the nursing homes. We have added extra info, lines 112-115, to clarify. The topic is also touched upon in lines 119-120. We hope that this sufficiently describes the intervention for the purpose of our article.

The main article describing the intervention study (reference 27 in this article) is recently accepted for publication in PLOS ONE and is expected to be published once it complies with outstanding technical requirements. This publication will enable the readers of our article to study the referenced article, where the setting of the intervention study is thoroughly described. This also means that in the case that our article is accepted, we will be able to update publication details for reference 27 in the subsequent proof-reading process.

'For all cases, clinical data were recorded at enrolment (day 1 in the treatment course) and at predefined days during the course of the acute illness, including delirium assessed with Confusion Assessment Method (CAM)' - death and delirium are mentioned in the stats section - can you provide more information as to how long patients were followed/checked for delirium and death?

- All clinical data were recorded until day 30. This info is now added in line 134. Information about death is added in lines 141-142.

Falls is also mentioned later in the manuscript but not at all in the methods.

- Thank you for pointing out this omission. The information is added in lines 138-141.

We also moved the sentence about dementia from the statistics section to this section (lines 143-144).

How long were participants follow-up for?
The follow-up in the intervention was 30 days. We hope this is clear with the above mentioned edits, including line 134.

Discussion - Any thoughts on why those with the best ADLs had the highest risk of receiving 3+psychotropic drugs? It is mentioned that it is not thought to be due to deprescribing as there wasn’t a relationship with number of drugs?

- Again, thank you for pointing out this omission in our argumentation. We have revised the relevant paragraph for clarity, especially adding lines 291-294.