Author’s response to reviews

Title: Variation between nursing homes in drug use and in drug-related problems

Authors:

Amura Francesca Fog (a.f.fog@medisin.uio.no)

Ibrahimu Mdala (ibrahimu.mdala@medisin.uio.no)

Knut Engedal (knut.engedal@aldringoghelse.no)

Jørund Straand (jorund.straand@medisin.uio.no)

Version: 1 Date: 12 May 2020

Author’s response to reviews:

Dear Editor,

Thank you for the opportunity to revise the manuscript and to resubmit it to BMC Geriatrics. We have addressed all comments from both reviewers. In the manuscript, revisions are shown by tracked changes. We also checked the editorial requirements and we hope that we addressed them in a proper manner.

On behalf of all authors,

Your sincerely,

Amura Fog

Point-by-point response to the comments from reviewer 1:

1) Reviewer: The article is presenting an analysis on drug use and drug related problems (DRP) across NH in Norway. Authors conclude that there is a large variability in use of psychotripics and opioids. Most relevant limitation of the article relates to the fact that it does not account for case mix of participating facilities. Characteristics of participants in different facilities can largely vary and this can explain the differences in drug use described. A higher prevalence of demented patients in a facility can give reason for a higher use of psychotropic medications. The lack of these data makes the paper difficult to interpret. Also, it might be interesting to know which organizational factors are associated with such a variability (presence of pharmacist in the facility? Academic vs non academic facilities? Etc..). These data might be necessary to drive interventions aimed at improving drug use

Response: First we want to make clear that this study is limited to nursing homes in one Norwegian municipality, namely Oslo, the capital of Norway. We agree that case mix at the participating nursing homes is important and that this may explain differences in drug use between
the sites. The only patient-characteristics recorded in our study were age and gender and we report
the age and gender distribution across the institutions in the Results section, lines 167 - 172.
Although we did not document the prevalence of dementia, the patient-mix was probably quite
similar across the participating nursing homes because admission to all nursing homes in this
municipality is according to the same medical criteria and regardless of income. We agree that
organizational factors might be associated with variability in the drug use among nursing homes,
however, all nursing homes in our study were non-academic and none had a pharmacist in the
facility.
We revised the text in the Discussion section lines 276 - 280.
“The NHs in Oslo are quite similar: They are publicly financed and administered by the same
agency, are non-academic institutions operating in the same regulatory and clinical practice
context. They are staffed with full-time nursing home physicians and registered nurses according
to the country standard. None of them had an in-house pharmacist. The patient-mix is quite similar
due to equal admission criteria.”

2) Reviewer: Was the assessment of DRP standardized across study sites and did pharmacists
receive specific training for the study? This is important to standardize the assessment procedure.

Response: We agree that it is important to give this information and we supplemented the
description of the study procedures in the Methods section lines 105 - 107:

“The MRs were conducted as a structured evaluation of each patient’s drug use and the assessment
of DRPs was standardized across the NHs. Training sessions were held for the involved
physicians, nurses and pharmacists before project start”.

3) Reviewer: It is not clear why the authors have chosen to focus specifically on several drug
classes (analgesics and psychotropics) rather than others.

Response: We focused on these drug classes because the vast majority of the nursing home
residents have dementia. Psychotropic and opioid drugs are commonly used off-label to treat
psychiatric and behavioural symptoms of dementia (BPSD), in spite of their limited effects and
poor safety. Their use is often considered potentially inappropriate and is associated with drug-
related problems.
We added the following text in the Methods section lines 125 – 128:

“We especially focussed on the use of psychotropic and analgesic drugs because their use,
although largely considered potentially inappropriate [9, 10] has increased in NHs [4, 5] and
because they are frequently involved in DRPs [3, 13, 14, 20, 21].”

4) Reviewer: Who assessed and collected data on drugs used? This is an important information
that should be provided.

Response: We agree that this information is important and it should be provided in the Methods
section, before the description of the procedure for identifying drug-related problems.
We added the following text in the Methods section lines 112 - 113:
“from the anonymized medication lists, the pharmacist retrieved data on the drugs used”.

We also added a more detailed description of the study methods, please see the revised text under comment 7).

Point-by-point response to the comments from reviewer 2:
This paper aims to describe variations in NHs based on information on use of drugs and drug-related problems. Even though the data is beginning to get old, the paper has value as it is a rather large cohort of NHs and describes "an unacceptable variation between NHs" which the authors relate to different and inappropriate drug prescribing cultures. Overall the paper is easy to follow, and logically presented. However, I have a few suggestions that the authors might consider;

5) Reviewer: Introduction L. 73-75 I would welcome a paragraph trying to explain why we see such substantial differences in drug use among these residents. References 12-15 do not represent the same geographical area, this should probably be re-written”.

Response: We corrected the placement of the references in the text and we added a short explanation on possible reasons for the variation in drug use.
The revised text in Introduction lines 73 – 77 reads:

“Substantial variations in drug use have previously been reported among residents in otherwise similar NHs with comparable patient populations [12 - 15], even if located in the same geographical area [13], and that institutions with high prevalence of drug use tend to use higher dosages [14], probably due to different prescription cultures and organizational factors at the institutions”

6) Reviewer: “Methods. It would be difficult to reproduce this study based on the information given in the method section, especially in relation to the identification of DRPs. Whenever using explicit criteria (START/STOPP is actually a mixture of implicit and explicit criteria), there is always several of these that is not applicable (due to lack of data). Most probably this would also influence the type of DRPs identified, but also determine which drugs that are associated to the different DRPs (If you are not able to provide detailed information, you should at least consider to discuss this limitation).”

Response: We agree that we should describe in more detail the study methods, instead of referring to a publication, and we have therefore supplemented the Methods section. We consider that the identification of drug-related problems in our study was not influenced by lack of data because the panel reviewed the entire list of medications in use and also had access to the patients’ medical record during the assessment.
The revised text in the Methods section lines 98 - 107 now reads:

“The NHs were recruited by invitation. Of the 51 NHs in Oslo municipality with long-term patients (n = 4,020), 41 NHs accepted to performed MRs at one, several or all the bed units in their institutions. All patients, and next of kin for patients with dementia at the participating bed units
were asked to participate in the study (n = 2,625 patients) with the exception of those terminally ill. Eighteen patients refused and 142 scheduled MRs were not performed because the patient died (n = 32), became terminally ill (n = 33), moved to another NH (n = 18) or due to logistical reasons (n = 59) during the study period. In average 60 patients per NH (range 19 – 136 patients per NH) underwent MR. The MRs were conducted as a structured evaluation of each patient’s entire drug use and the assessment of DRPs was standardized across the NHs. Training sessions were held for the involved physicians, nurses and pharmacists (n = 5) before project start.”

We have also made some minor revisions in the text from line 108 to line 118 to ensure a more accurate description of the methods used.

7) Reviewer: There is nothing wrong about grouping the NHs in quantiles based on patients mean drug use, as you have done. But, did you consider to use a cluster analysis (taking more variables into account) to group the nursing homes (based on the dendrogram you could easily decide on number of clusters)?

Response: We thank the reviewer for suggesting cluster analysis, in particular the dendrogram, in grouping the nursing homes (NHs). Our choice of the quantiles was driven by our desire to have four equally sized groups with some NHs using more drugs than others. This was a natural way of grouping and summarizing data with extreme users (outliers). In addition, grouping of NHs into quartiles made it more easy to identify and compare NHs that were low users of drugs from high users. However, a dendrogram was given much consideration at the beginning of the analyses but we dropped the idea in favor of the quartiles. Using the dendrogram, the clusters that we identified were as shown in the figure below:

Unfortunatelly the figure we have prepared could not be inserted into this document.

Figure: A dendrogram based on patients’ mean drug use for 41 nursing homes (numbers along X-axis represent the different institutions) in Oslo

Looking at this dendrogram, we can identify four clusters that occur at about the same distance (height), that is, below 1. The largest of these clusters comprises of the following 14 NHs: 1, 6, 34, 14, 15, 13, 4, 29, 22, 26, 40, 37, 32 and 30, while the smallest cluster comprises of only 4 NHs: 9, 36, 27 and 18. However, we also have NH 28 (an outlier) because it joins all the other NHs at a much higher distance (height). Therefore, we decided to base the grouping of the NHs on the quartiles.

8) Reviewer: You do not include patients >90 yrs in your material, please provide some information about which patients that were eligible.

Response: We have by mistake omitted to write that the 90 years represented the upper range of the mean age per nursing home. The correct mean age for the total population are 85.6 years (range 36 – 108 years). Of the total population, 979 patients (39.7%) were 90 years or older. We revised the text in the Results section lines 167 – 171 as follows:

“The mean age of the residents was 85.9 years (range 36 – 108 years). The age distribution was comparable across the NHs (mean age per NH was 85.9 years, range 61.3 – 90.0 years per NH),
except for two institutions especially designed for younger people with dementia (61.3 and 68.4 years, respectively).

9) Reviewer: Results. I think most of the results are reported adequately. Line 159; last part of sentence could be deleted. From line 165 and forward, please be consistent with number of decimals reported.

Response: We have deleted the last part of the respective sentence (line 178) and we corrected the number of decimals to ensure consistency.

10) Reviewer: Discussion. L194. Based on information in Table 2, I think you also should include paracetamol (or change opioids with analgesics).

Response: we changed opioids with analgesics (line 213).

11) Reviewer: L202. By taking a quick look at your references, I also found that reference 35 gives detail information about DRPs for four different rural nursing homes.

Response: We thank for making us aware of this omission, the revised text in the Discussion section lines 220 - 224 now reads:

“Further, the study documented that the rates of DRPs varied up to seven fold (from 0.5 to 3.4) between the NHs. To the best of our knowledge, two medication review studies previously reported variation in DPRs between NHs, one in two urban NHs, from 3.0 to 5.5 mean DRPs per patient [20] and another study in four rural NHs, from 2.7 to 5.6 mean DRPs per patient [35].”

12) Reviewer: L204-206. As stated in the method section; if identification of DRPs were only based on scrutinizing drug lists based on the three criteria, it is not surprising that the number of DRPs are somewhat lower.

Response: In addition to the explicit criteria and the drug-drug interaction database, DRPs were identified and assessed taken into consideration also clinical information from the patient’s medical record, including clinical status, lab values and functional assessments.

13) Reviewer: Strengths and limitations. You state here that the explicit criteria were updated after the study have started; why should this influence your results?

Response: We do not believe that the revised explicit criteria would have changed our results, however, because they are more comprehensive than the previous versions, their use would have probably increased the number of DRPs identified by the pharmacist alone.

14) Reviewer: Reference. Please update this according to guidelines. Reference 25 should for instance be translated.

Response: We have updated the references.
15) Reviewer: Tables and Figures Figure 1, footnote - please change Table 1 to 2

Response: We have corrected the footnote.

We have made the requested corrections to meet the journal's requirements: we moved the Figure after the References and we completed the Declaration sections.