Author's response to reviews

Title: Sedative load of medications prescribed for older people with dementia in care homes

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Author's response to reviews: see over
Responses to reviewers’ comments on “Sedative load of medications prescribed for older people with dementia in care homes”

Please find below detailed responses to the reviewers’ comments on the above paper. We thank the reviewers for their comments which have contributed to the revision of the manuscript. The page numbers referred to in the referees’ comments relate to those used by the referees in their reports. However, the page numbers in our responses relate to the redrafted version. Further changes made in response to the reviewers’ comments and any additional changes have been highlighted in the text using the tracked changes facility in Microsoft Word.

Response to referee 1

General comments

This is an interesting manuscript that investigates the pattern of sedative use in older people, especially those that are most vulnerable with dementia. The authors have employed data from a longitudinal study in residents of aged care facilities and applied the “sedative load model”. This is an important question as it relates to potentially significant medication-related harms for older people. The strength of the study is the use of patient medication administration which ensures that they capture relevant and complete medication data. Perhaps a weakness is the diagnosis of dementia which was essentially based on a clinical or “recorded” diagnosis within patient notes. There was limited information about severity of dementia.

We acknowledge the referee’s comment that the diagnosis of dementia was essentially based on a clinical or “recorded diagnosis” within the patient notes and that there was limited information about the severity of dementia. We have included a statement to this effect in the discussion of the limitations of the study (page 14). The original study protocol for the EVIDEM-EOL study had specified the use of a validated measure of cognitive function to identify potential participants. However, during recruitment it became apparent that completing a formal assessment could have unintended consequences for participants with some care home managers potentially wanting to use the results from a validated assessment of dementia as evidence to justify raising a resident’s fees. Following discussion with the steering committee, it was therefore decided that it was appropriate to include residents identified either through a documented diagnosis of dementia within residents’ care home notes or by senior care home staff as having cognitive impairment consistent with a diagnosis of dementia. 75% of people resident in care homes have dementia and of these 35% have advanced dementia; a recent BMJ paper by Richards and Brayne (BMJ 2010; 341:doi:10.1136/bmj.c4670) on Alzheimer’s disease observe that as a diffuse clinical syndrome that involves the gradual accumulation of multiple pathologies, arising from multiple interlocking risk factors, a diagnosis is less important than an understanding of its impact on function. The care notes and care home staff assessment of residents’ ability to function identified those residents whose dementia affected their functional and cognitive ability and arguably is a clinically more useful way of identifying residents living with the consequences of dementia. The challenges of recruiting people with dementia to studies and our rationale for the approach taken has been discussed by some of the authors in another paper (Goodman, C., Baron N., Machen, I. et al. (2011) Culture, consent, costs and care homes: Enabling older people with dementia to participate in research. Aging & Mental Health, 15 Issue 4, 475-481).
Discretionary revisions

1. The authors refer to the work of Hilmer et al on total drug burden, which combines both sedative and anticholinergic medicines as well as considers drug dose regimen. How should this study be considered in light of the studies investigating the drug burden index (DBI) using a sedative load model that simply counts medicines and does not consider dose.

*We have highlighted within the discussion of the limitations of the study (page 14) that the sedative load model does not consider doses and frequencies of medications. However, each of the models used to quantify the cumulative effects of taking multiple drugs with sedative properties (the sedative load model, the Sloane model, the DBI and the central nervous drug system model) have advantages and disadvantages associated with their use, with each model differing with respect to the specific drugs or drug classes considered, the sedative ratings assigned to each drug, the inclusion or exclusion of drug dose in the model, and their likely ease of use in clinical practice. Thus far use of these models has been restricted to pharmacoepidemiological research; none have been applied prospectively in clinical practice. Whilst inclusion of dose in the DBI represents one of the strengths of this model, calculation of the score does not utilise a reference dose specific to older individuals. Furthermore, unlike the sedative load model, the DBI does not include ratings of sedative drugs. Studies which utilise the DBI and those which utilise the sedative load model should therefore be considered in the context of their strengths and limitations. The reference to the work of Hilmer et al on total drug burden was included in the introduction to indicate that a number of models are available to quantify drug load. We have added some further references to the introduction (page 5), including a commentary which compares the different methods used to quantify the cumulative effect of taking multiple drugs with sedative properties (Taipale et al., 2010).*

2. The authors state “...no studies which examine the use of the sedative load model to examine prescribing of sedative medications in residents of residential homes have been conducted to date”. While no study has used this exact model – a range of other models including DBI such as...


   *We have amended the preceding sentence to “Drug Burden Index (a measure of a person’s exposure to anticholinergic and sedative medications) has been used to examine exposure of residents of residential aged care facilities in Australia to medications with anticholinergic and sedative properties” and have added the references suggested by the referee (page 5).*

3. This study only examined data for people living with a diagnosis of dementia – did the authors consider a comparison between the sedative load in older people with and without a diagnosis of dementia?
This study comprised a retrospective analysis of medication data collected for older people with dementia in six residential care homes in England who participated in the prospective longitudinal EVIDEM-End of Life (EoL) study. As medication data were not collected for residents who did not have a diagnosis of dementia, it was not possible to compare sedative loads in older people with and without dementia.

4. Indicate the time period over which data were collected in the Methods section.

Details of the time period over which data were collected have been added to the Methods section (page 6).

5. This is an observational study – match the conclusions to the aims of the study.

The aims of the study were to determine the sedative load and the use of sedative and psychotropic medications among older people with dementia living in residential care homes. In the conclusion we have indicated that the sedative load scores were similar across each of the six participating care homes and were lower than previously reported in other care home settings. We have also discussed that residents with dementia in this study were more frequently prescribed drugs which had sedation as a prominent adverse effect and/or contained a sedating component rather than primary sedatives. Antidepressants, predominantly SSRIs, were most frequently prescribed, while prescribing levels of hypnotics and anxiolytics were lower.

6. Table 1 – there is no need to report age to 2 decimal places

We have amended table 1 so that age is reported to 1 decimal place.

7. Tables 1 – 3 I am unsure of the rationale for presenting data for each of the homes separately at each time point – is this the best way to present the data? Is there merit in combining these data and perhaps using a figure?

We have detailed the data in these tables for each of the six homes separately to allow the reader to consider the demographic profile, sedative load and prescribing of medications at the individual care home level. This enables the reader to identify similarities and differences in the data and to verify the discussion of the results obtained.

**Response to referee 2**

General remarks

The study determined prevalence of sedative load in residential care home residents which is a valuable addition to the current research focusing on sedative load in long-term care facilities and among community-dwelling older people. Also, pattern of psychotropic drug use in this population adds to current research. However, the authors need more precision in their medication-related definitions, and description of medication administration charts as a source of medication data.

Major compulsory revisions
Background

1. Sentence in the second paragraph: “The over-use of psychotropis drugs (antipsychotics, hypnotics and anxiolytics)...” implies that antidepressants are not included in the definition of psychotropic drugs. This is not consistent with Methods section.

   *We have amended this sentence to read “The over-use of psychotropic drugs (antipsychotics, antidepressants, hypnotics, and anxiolytics) has been a particular concern in the literature on prescribing and use of medicines in care homes”; it is now consistent with the Methods section.*

Methods

2. Major methodological question is description of “medication administration records”. What are those, who administers medications, staff? For determination of drug use, were those records screened for a day or for a time period, like a week for this study?

   *In order to clarify the above, we have included the following in the Methods section “Medication data for each participating resident were collected at baseline and at two further time-points using medication administration records obtained from the care home notes which detailed the medications prescribed and administered by care home staff over the four-week period which coincided with each data collection time-point. The maximum number of medications prescribed for and administered to the resident at any one time during this four-week period was utilised to determine drug use at each data collection time-point”.*

3. How was regular use of a medication defined?

   *We have included a definition of regular use of medication in the Methods section (page 7).*

4. Were participants asked for written consent to participate in the study?

   *We have included further detail regarding consent in the Methods section (page 6). Written informed consent to participate in the study was obtained from those eligible residents who were considered to have capacity to consent. For those residents deemed not to have capacity to consent for themselves, written assent was obtained from a personal consultee who, based on his/her knowledge of the resident, could provide an opinion as to whether the resident would have consented to his/her care notes being reviewed.*

5. How were co-morbidities determined, from medical records?

   *Co-morbidities were determined from residents’ care home notes. We have clarified this in the Methods section (page 9).*

6. Standardize use of the term “hypnotics” or “sedative hypnotics” if the meaning is the same.
We have standardized this such that the term “hypnotics” is used throughout the text.

7. Definition of primary sedatives is unclear. Do you mean Group 1 drugs, as in the sedative load model, or hypnotics and anxiolytics (page 10, results)?

We acknowledge that our definition of primary sedatives was unclear in some parts of the text. We have therefore amended accordingly to indicate that primary sedatives include all Group 1 drugs.

Results

8. In the methods, it is stated that all 115 residents had dementia. Sentences “At baseline, eighty-six had a recorded diagnosis of dementia in their care home notes... According to care home notes, a specific cognitive test such as the Mini-Mental State Examination had been administered for 23 residents” are unclear. Now other 115-86=29 residents were diagnosed? For those 23 residents who had been administered MMSE, was the test result indicative of cognitive decline?

The inclusion criteria for participation in the study were: care home residents who were 65 years of age or older, and who had a documented diagnosis of dementia, or who were determined by senior care home staff as having cognitive impairment indicative of dementia. Therefore 86 residents had a diagnosis of dementia in their care home notes, while the other 29 residents were determined by care home staff as having cognitive impairment indicative of dementia. Only 23 residents had had the MMSE administered. We have amended the text in the Results section (page 8) to clarify this. We do not have MMSE scores for each of the 23 residents at each of the three data collection time-points therefore we are not able to determine whether these residents experienced cognitive decline or whether their cognitive function remained stable.

9. The study analysed medication administration charts as a source of drug use data. Authors should consider do these medication administration charts describe “prescribed medications” or “actually used medications” because often all prescribed medications are not used by a patient. Now the wording used in the manuscript is “prescribed medications”.

The medication administration records obtained from the care home notes detailed the medications prescribed and administered by care home staff. We acknowledge that the use of the term “prescribed medication” throughout the text may be misleading as we are referring to the medications prescribed for and administered to the residents, and we have therefore amended the text as appropriate to indicate that we are considering the use of medications (i.e. prescription and administration).

Minor essential revisions

1. Currently, in the abstract there is no mention of prevalence of antipsychotic prescription which would be of interest for the readers.

We have included a sentence discussing prevalence of antipsychotic use in the abstract.
2. Please standardise writing style of “Sedative Load Model/sedative load model” throughout the manuscript.

*We have standardised “sedative load model” throughout the manuscript.*

3. Were there any differences between participants and non-participants?

*We are not able to determine whether there were any differences between participants and non-participants as we did not seek or obtain consent from non-participating residents or their consultees to collect any information about these individuals.*

4. In results, paragraph starting with “prescribing of regular medications is outlined in Table 3” should be divided into sub-paragraphs, for example, the second starting with antidepressant use, and the third starting with hypnotics and anxiolytics.

*This has been amended in the manuscript (pages 9 – 11).*

5. In results, sentence “prescribing of antidepressants across the care homes was similar” is misleading (page 11). If this sentence is comparing prescribing at time-point 3, then prescribing varies from 25% to 64.3% according to table 3.

*We have removed this sentence and have replaced it with “Use of antidepressants ranged from 25.0% in care home 2 to 64.3% in care home 3”*

6. “Whilst some studies have reported that patients with dementia are frequent users of antipsychotics and hypnotics [20,40], this study found that across all care homes, residents were more frequently prescribed antidepressants and less routinely prescribed antipsychotics and hypnotics and anxiolytics”. Please mention that one reason for this difference may be that previous studies have measured both regular and when-required medication use.

*We have amended this as per the referee’s suggestion.*

7. In results, the sentence “However, in care home 2, primary sedatives were not prescribed (Table 5)”. However, table 4 indicates that at time-point 3, there are users of TCAs (6.3%). Again, be consistent with definition of primary sedatives.

*This sentence has been amended to “in care home 2, hypnotics and anxiolytics were not administered”.*

8. Sentence in the discussion, “These medications, which are classified as primary sedatives, contributed extensively to the resident’s sedative load score and may have negatively impacted on their health and well-being” seems too overall.

*This sentence has been removed from the discussion.*

9. In discussion, “Previous studies have reported that patients with dementia were most frequently prescribed antipsychotics...”, does this mean that “of psychotropic drug groups”?
This sentence has been amended to indicate that this means that previous studies have indicated that antipsychotics were the most frequently prescribed psychotropic medications for patients with dementia (page 15).

10. Consider that trazodone may also be used for the treatment of insomnia which may explain some differences across care homes (low use of hypnotics but high use of trazodone)

We have included a sentence to indicate that trazodone may be used for treatment of insomnia.

11. In Table 4, can you add % of users of each drug class (antipsychotics, antidepressants, etc.)?

Table 4 has been amended to include numbers and % of users of each drug class.

12. In table 5, “trazadone” should be changed to “trazodone” to be consistent with the text.

We have changed the spelling of “trazadone” to “trazodone” in table 5.

13. In table 5, “For residential care home residents with dementia” to the title of the table.

We have amended the title as suggested by the referee.

Response to referee 3

No major or essential revisions

Discretionary revisions

1. I’m not sure whether your data is capable of this but the prevalence of sedation is fairly stable throughout the study, what would be interesting is the admission status. Basically I suspect you will find this to be a patient population issue not a care home specific matter.

We agree with the referee that the prevalence of sedation is likely to be a patient population issue rather than a care home specific matter but as suggested by the referee it is not possible to draw any conclusions regarding sedation and admission status using our data.

2. Your analysis alludes to the positive effect on prescribing of affiliation to a memory clinic – it would have been interesting to look at GP notes to determine the origin of sedation, hospital/community – specialist/generalist

We agree with the referee’s comment but we only had access to the residential care home notes and care plans for residents. We did not have access to GP notes.
3. On page 13, I object to the term “frequent users” I prefer “frequently prescribed”

   *We have amended this as per the referee’s suggestion (page 14)*

4. What you do show is that a significant proportion of prescriptions are lower dosage, the question is unanswered whether this is helpful or harmful and I think you could be asking for formal trials of low dose sedation in dementia to see if there could be established a constructive usage. Whilst I do not condone unnecessary sedation at all there is a possibility that a possible benefit of low dose treatment is being missed in the present approach.

   *The sedative load model does not include the dose of the medication in calculating the sedative load score. It assigns sedative ratings to drugs based on their sedative potential. We have included a statement in the discussion to the effect that formal trials of psychotropic drugs with low sedative loading in dementia are required to determine whether there is any possible benefit.*

5. It is striking that new atypical are preferred over older agents, is this because practitioners understand them to be less problematic or just “prescribing fashion”.

   *We have included the following in the discussion “Overall, atypical antipsychotics were more commonly prescribed used than conventional antipsychotics, reflecting the evidence that these medications are superior in controlling the behavioural and psychological symptoms of dementia [49], contribute less to the sedative load score and are associated with fewer extrapyramidal side-effects”. However we do acknowledge that there may also be an element of “prescribing fashion” and have added mention of prescribing trends.*

6. It continues to be disturbing that diagnoses are effectively presumed and that severity/staging is not standardised. Mention of this in your discussion would have been interesting.

   *We have included a paragraph discussing this point in our discussion (page 16).*