Author's response to reviews

Title: Excessive daytime sleepiness and falls among older men and women: cross-sectional examination of a population-based sample.

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Dr. Geeske Peeters
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**Manuscript title:** Excessive daytime sleepiness and falls among older adults: cross-sectional examination of a population-based sample.  
**Authors:** Amie C Hayley, Lana J Williams, Gerard A Kennedy, Kara L Holloway, Michael Berk, Sharon L Brennan-Olsen and Julie A Pasco.

Dear Dr. Peeters,

Thank you for considering the revised version of the original research article for publication in BMC Geriatrics.

We thank you for your suggestions for edits to the submitted manuscript and have found the critiques to be helpful in further developing and improving the quality of the manuscript. We have addressed all aspects of the comments and concerns raised, and have made some additional typographical amendments to the text in light of these suggestions. Please find attached to this letter our detailed response to the comments raised by the reviewers.

Accordingly, we have uploaded a copy of the original manuscript marked with all the changes made during the revision process. The new text is underlined while the crossed-out text refers to the deleted original text. In addition, we have uploaded a clean version of the amended text.

We would like to take the opportunity to thank you for allowing us to resubmit a revised copy of the manuscript, and look forward to hearing from you in due time regarding our submission and to respond to any further questions and comments you may have.

Many thanks,

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Reviewer 1.

The analytical strategy is confusing. This study collected a comprehensive set of variables; however, when performing statistical analyses, the principle of covariate selection is confusing. In table 1, the authors summarized correlates of EDS. This is a standard approach to identify potential confounders when examining the association between EDS and falls. Theoretically, only factors which have data-based association with EDS or covariates that have been recognized as risk indicators for falls could be and should be put into the multiple logistic regressions. In line 211-214, the authors mentioned that walking aid, smoking status, alcohol intake, sedative medication, physical activity and nocturia were included in the multivariate analyses to examine the independent effect of EDS on falls in females. I am wondering why these covariates were chosen instead of those which showed significantly uneven distribution in the EDS status, such as diabetes (table 1).

We agree that the univariate analyses should provide indication of possible contributory variables. We have now re-run the analyses including only the variables ‘walking aid’, ‘nocturia’ and ‘diabetic status’ as the study covariates (other variables, smoking etc. were not included for analyses), and the results section has been amended as follows (unadjusted OR is still reported);

‘EDS was associated with an increased risk of a fall (unadjusted OR= 2.19, 95%CI 1.20-4.01, \( p=0.01 \), and this was sustained following adjustment for the use of a walking aid (adjusted OR= 1.93, 95%CI 1.04-3.60, \( p=0.04 \)). These findings were independent of nocturia and diabetic status (Table 2).’

We have also now presented these analyses in an additional table (for both men and women, now entitled Table 2).

In parallel, although EDS did not correlate with fall in the univariate analysis in male, the association between EDS and falls may be compromised by other covariates. In addition, the risk for fall, estimated with The Elderly Fall Screening Test (EFST) in the present study, is also of clinical interest and importance. When examining the relationship between EDS and EFST in males, the authors only mentioned age confounded this association (lines 245-248). How about the contribution of other significant correlates of EDS in male? For example height, weight, use of walking aid, smoking and mood disorder (table 1).

Initial univariate assessment of the scores on the EFST and EDS among men revealed a trend towards significance (\( p=0.06 \)). Given that men with EDS were older than those without EDS (Table 1), age was included in a multivariable model. This analysis revealed that age fully explained this relationship, and thus this was entered as the first (and only) covariate for assessment. Given this finding, it was decided that additional assessment of peripheral covariates would not add any additional information.

Therefore, an additional table that summarizes results derived from multiple logistic regressions is suggested. In this table, the dependent variables are suggested to include both falls and EFST. Stratifying the analyses by gender is also encouraged. The rationale for selecting eligible covariates should be stated. In addition, all eligible covariates should be entered simultaneously in the multivariate regression models.

According to the reviewer’s suggestion, we have now included an additional table to display the results of the multivariable regression models where covariates have been entered sequentially. This
includes one table which combines the models presented for both men (EFST scores) and women (falls history). This table presents the fully adjusted models only (now labelled as Table 2).

We have retained the statistical method of entering potential covariates into the model sequentially. This method did not alter the reported findings of the revised multivariable statistical assessments (for women).

2. This study is unique in demonstrating gender difference. However, the mechanism that underlies this gender-specific finding is not fully discussed. Please expand the current paragraph (lines 291-294) that should address this issue.

We have now extended this paragraph to include further discussion of the possible mechanisms underlying this association. The sentence now reads as follows (included text is indicated with underline):

‘Among men, no relationship was detected between EDS and falls history, and only a trend towards significance was noted between EDS and falls risk as assessed by the EFST score. These findings, in part, mirrors previous research which has typically suggested a lower overall prevalence of falls among older men compared to women [35, 41], and reported that female gender represents a risk factor for falls [35]; however this finding is not universal [10]. Singular aspects of the EFST have been shown to be accurate predictors of falls risk in men, such as slow and/or unsteady or gait [42], however balance and/or gait assessments alone are not considered effective predictors of relative falls risk [43]. We acknowledge that we did not observe an association between EDS and falls, and suggest that this finding may, in part, be due to underreporting of falls by the male participants. Furthermore, as only a small proportion of men reported both a fall and EDS, we cannot exclude the possibility of a type 2 error. Future research would benefit from corroborating both objective and subjective fall records in order to recognise any possible sources of personal bias in responses.’

Minor Essential Revisions

1. In abstract, I suggest use interquartile range directly instead of the acronym of IQR.

The methods section of the abstract has now been amended to define the interquartile range directly (acronym has been removed), and now reads as follows:

‘Methods: This study assessed 367 women aged 60-93 years (median 72, interquartile range 65-79) and 451 men aged 60-92 years (median 73, interquartile range 66-80) who participated in the Geelong Osteoporosis Study between the years 2001 and 2008. Falls during the prior year were documented via self-report, and for men, falls risk score was obtained using an Elderly Fall Screening Test (EFST). Sleepiness was assessed using the Epworth Sleepiness Scale (ESS), and scores of ≥ 10 indicated EDS. Characteristic differences between those with and without EDS were assessed using appropriate univariate analyses, and differences among those with and without EDS in regard to falls were tested using logistic regression models.’

2. Some acronyms are not necessary, e.g. BSD in line 80, ABS in line 170, SEIFA in line 171 and IRSAD in line 172.

These acronyms have now been removed.

3. Information of figure 1 has been well addressed in the context. I suggest delete it.

We thank the reviewer for this suggestion and have now removed the figure and have removed reference to the figure in text.
4. In line 260, the gender for respective prevalence of EDS should be added.

We have now added a sentence in the introductory paragraph of the discussion to highlight the prevalence of EDS for men and women for this study. The sentence reads as follows (amended section is underlined);

‘Over one tenth of men and women aged >60 years assessed in this study report clinically significant levels of EDS. The results from this cross-sectional study suggest that for women, EDS is associated with an approximate two-fold increased likelihood of reporting at least one fall during the previous year, independent of a number of confounding factors. Further, women with EDS were more likely to report a fall occurring whilst located outside, whereas women without EDS were more likely to report a fall whilst located inside. No association was observed for men with regard to EDS and falls history; however, a trend towards significance was noted between EDS and an increased risk profile for falls as assessed by the EFST. Both men and women reported falls occurring most frequently as a result of tripping and indicated that soft-tissue injuries were the most common reported injury sustained as a result of the fall.’

5. I am not sure whether these words had been misspelled. Please make a check. Line 265, "compounding factors"; line 284, "come limitations"

We thank the reviewer for highlighting these typographical errors, and we have now corrected the text.

6. In lines 215-221, p value for the interaction term of EDS and antidepressant use should be illustrated to justify the performance of stratified analyses by antidepressant use.

We have now added the p value to justify stratification by antidepressant use in the results section and this now reads as follows:

‘Initial multivariate modelling revealed antidepressant use (current) as an effect modifier (p < 0.001 for the interaction term).’

Discretionary Revisions 1. Because ‘gender difference’ is the core finding of this study, the authors may consider adding this keyword into the title.

We have amended the title of the manuscript to include ‘men and women’, and it now reads as follows:

‘Excessive daytime sleepiness and falls among older men and women: cross-sectional examination of a population-based sample’
Reviewer 2

In my opinion, the paper would benefit from the inclusion of a table (manuscript or appendix) presenting the odds ratios and 95% confidence intervals of the unadjusted and multivariable adjusted analyses concerning the association between excessive daytime sleepiness and falls in the previous year for men and women and the relationship between excessive daytime sleepiness and the fall risk (EFST) for men. Hereby, please indicate clearly the respective covariables used in each logistic regression model.

We thank the reviewer for this suggestion, and in light of these comments and the suggestion from Reviewer 1, have now included an additional table outlining the fully adjusted regression models (not the unadjusted) for both men and women (now labelled as Table 2), which display the relevant OR and 95%CI.

2. Please provide in the abstract some information about the statistical methods used for the calculations.

We have now amended the abstract to briefly mention the statistical methods used and it now reads as follows (amended section is underlined):

‘Methods: This study assessed 367 women aged 60-93 years (median 72, interquartile range 65-79) and 451 men aged 60-92 years (median 73, interquartile range 66-80) who participated in the Geelong Osteoporosis Study between the years 2001 and 2008. Falls during the prior year were documented via self-report, and for men, falls risk score was obtained using an Elderly Fall Screening Test (EFST). Sleepiness was assessed using the Epworth Sleepiness Scale (ESS), and scores of $\geq 10$ indicated EDS. Characteristic differences between those with and without EDS were assessed using appropriate univariate analyses, and differences among those with and without EDS in regard to falls were tested using logistic regression models.’

3. I would suggest more discussion around potential mechanisms of the association between sleepiness and falls/risk of falls.

Additional assessment of possible mechanisms underlying this association has now been added to the discussion section. Specifically, we have expanded the paragraph discussing possible explanations for the lack of associations between EDS and falls for men, which provides further evaluation of these findings. This section now reads as follows:

‘Among men, no relationship was detected between EDS and falls history, and only a trend towards significance was noted between EDS and falls risk as assessed by the EFST score. These findings, in part, mirrors previous research which has typically suggested a lower overall prevalence of falls among older men compared to women [35, 41], and reported that female gender represents a risk factor for falls [35]; however this finding is not universal [10]. Singular aspects of the EFST have been shown to be accurate predictors of falls risk in men, such as slow and/or unsteady or gait [42], however balance and/or gait assessments alone are not considered effective predictors of relative falls risk [43]. We acknowledge that we did not observe an association between EDS and falls, and suggest that this finding may, in part, be due to underreporting of falls by the male participants. Furthermore, as only a small proportion of men reported both falls and EDS, we cannot exclude the possibility of a type 2 error. Future research would benefit from corroborating both objective and subjective fall records in order to recognise any possible sources of personal bias in responses.’
We have also included the following paragraph in the discussion section (amended text is underlined):

‘We report that the association between EDS and falls among women is observed only among non-users of antidepressant medications, however, and thus the role of this relationship in the expression of falls risk among affected individuals is unclear. It is possible that other drug classes, as well as drug interactions are contributing to these findings. As a comprehensive examination of medication classes and drug interactions were beyond the scope of this study, further research would benefit from direct and comprehensive assessment of the association between EDS, antidepressant and other medication use and falls risk.’

4. In the interest of the reading flow, maybe e.g. „among men“ and „among women“ is more advantageous than „men:“ and „women:“ in the results section of the abstract?

This has now been amended to improve readability.

5. Please be consistent in your use of „year“ or „yr“

We thank the reviewer for highlighting this inconsistency. We have now amended the abstract and text to refer to ‘year’ only.


This typographical error has been amended

7. Page 8, line 165: „:“ instead of „;“. 

This typographical error has now been amended