

Author's response to reviews

Title: The association of blood lead concentrations and mortality in older women, the Study of Osteoporotic Fractures:prospective cohort study

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Author's response to reviews: see over

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The Environmental Health
Editorial Team

Dear Sir/Madam,

Thank you for the second review of our manuscript "MS: 3047867652304652, The association of blood lead concentration and mortality in older women: the Study of Osteoporotic Fractures, a prospective longitudinal study". We revised the manuscript along your suggestions. We have addressed each comment below.

Editor Comments:

1. Comment. We note that the stepwise models exclude some established risk factors. We would like to know to which degree they affect the results

Response: We have revised the methods section to reflect the strategy for hazards model building which is now based on the biological plausibility and referenced in literature instead of stepwise covariate selection. We have added a new table No. 4 which gives the hazards ratio for each variable considered for analysis. The results section also has been revised to reflect final covariate selection for models.

2. Comment: Also, please use the word 'concentration' instead of the imprecise word 'level' in the manuscript title. We prefer SI units, and ug/dL is no longer a proper unit for the blood-lead concentration. We will accept ug/L, provided a conversion factor is indicated for an SI unit (umol/L).

Response: The word 'level' has been replaced with 'concentration' in title. As advised we have added the SI units in parenthesis whenever lead units in ug/dL are mentioned.

3. Comment: Please also ensure that your revised manuscript conforms to the journal style (<http://www.ehjournal.net/info/instructions/>). It is important that your files are correctly formatted.

Response: We have formatted the revised manuscript files to conform to the journal style.

4. Comment: Among necessary changes, please adjust the title in regard to the use of capital letters and with a subtitle that indicates the study type (e.g., prospective cohort study).

Response: We have corrected the title in regard to the use of capital letters and with a subtitle that indicates the study type (e.g., prospective cohort study).

5. Comment: The corresponding editor on the title page should be indicated by a symbol such as ^{Â§} in superscript after his/her name and a line on the page reading ^{Â§}Corresponding author.

Response: The corresponding author on the title page is now indicated by a symbol (*) in superscript after her name and a line on the page reading (*) Corresponding author.

6. Comment: Please remove all contact information as presently printed on the page.

Response: All contact information as printed on the title page has been removed.

7. Comment: The pagination should be removed

Response: The pagination has been removed.

8. Comment: The proper symbol should be inserted instead of \leq .

Response: We have replaced the symbol \leq with \geq in the text, however in figure.1 while making graph in STATA program the statistical program code did not accept the symbol \geq and we had to substitute it with the sign \leq .

9. Comment: Please remove yellow highlighting (although helpful at an initial stage of review).

Response: The highlighting has been removed.

10. Comment: The Abbreviations section (where the terms should be listed in alphabetic sequence) should start on a new page, to be followed by competing interests, authors' contributions, etc

Response: The Abbreviations section has been corrected, it now starts on a new page, and terms are now listed in alphabetic sequence. This section is followed by sections of competing interests, authors' contributions, etc.

11. Comment: Please also see the instructions for authors as to the proper formatting for the references. The references should have one space between the numbers and references and not be tabbed

Response: We downloaded the style file from Biomed Central website and formatted the references with one space between the numbers and references and removed tabs.

12. Comment: All tables for tables and figures need to be in a closed cell format with the borders showing.

Response: All tables for tables and figures are now in a closed cell format with the borders showing.

13. Comment: On the manuscript record page on the server, please list only middle initials for the authors. If you change the manuscript title (as we suggest), please make sure that it's reflected on the server record as well.

Response: On the manuscript record page on the server, we have changed the authors' list and only middle initials for the authors are now displayed.

Reviewer's comments

Reviewer 2

1. Comment: In general, a biologically driven analysis approach that includes co-variables if they are significant in the model or if they change the association between the exposure and outcome of interest is preferable to one that is solely based on significance of the variable such as stepwise backward elimination. This is particularly true for well established risk factors such as smoking and diabetes. Thus, it would be preferable to report the results in Table 4 and the abstract after full adjustment. For example CHD mortality HR as 3.08 (95% CI, 1.24- 7.65) $p < 0.016$].

Response: We have revised the methods section to reflect the strategy for hazards model building based on the biologically driven analysis approach that includes co-variables that change the association between the exposure and mortality instead of the previous one that was based on significance of the variable such as stepwise backward elimination. We have added a new table No. 4 which gives the hazards ratio for each variable considered for analysis. The results section also has been revised to reflect final covariate selection.

2. Comment: In adding the full analyses, on the top of page 11 in results the authors appear to mean CVD not CHD: "However adding these risk factors to the CHD model decreased the HR and the statistical significance [1.78(95% CI, 0.92- 3.44), $p < 0.087$]."

Response: We apologize for the omission, the sentence has been changed.

3. Comment: In the last sentence of conclusions, I am unclear what "levels below current level of concern." Means.

Response: The last sentence in conclusions has been revised.

Thank you again for the review. Your suggestions have helped us to improve our manuscript.

Sincerely

Naila Khalil