Author’s response to reviews

Title: Environmental risk factors for dementia: a systematic review

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Author’s response to reviews:

Reviewer 1

This is well-written review paper.

OUR RESPONSE: We thank the reviewer for their positive comment.

I only have a couple of minor comments to share with the authors.

1. Different studies included in the review might use different criteria to define dementia. It is unclear how the authors addressed this. Also, many studies may have poor data quality for air pollution or for other risk factors. These may noted in the text. Furthermore, many studies may not have adequate controls, which may exaggerate the effect size of air pollution or other risk factors on dementia. This should also be noted in the text.

OUR RESPONSE: The use of different diagnostic criteria for dementia is a ubiquitous problem in epidemiological studies, as is measurement error in exposures or inadequate controls. We have added some consideration of these problems in the limitations section of the discussion:
“…exposures which were investigated in more than one study were also measured in a variety of ways, sometimes with variable quality.” (pp. 15-16)

“There was a similar diversity of methodologies (and diagnostic criteria) used to identify people with dementia and it is important to consider whether any of these may introduce bias.” (p. 17)

“An additional important point is the adequacy of controls in case-control studies – there was some variability in the extent of matching with people with dementia.” (p. 17)

2. Conclusions: The first sentence seems to be not consistent with the two sentences followed. Please double check.

OUR RESPONSE: We have now revised the concluding paragraph of the manuscript for clarity. It now reads:

“In conclusion, the published evidence concerning specific environmental risk factors for dementia is generally not strong. However, there seems to be little role for most metals or other trace elements, occupational exposure to lead, inks/dyes, paints/stains/varnishes, gasoline/fuels/oils, liquid plastics/rubbers, vibratory tools, or climate in determining dementia risk. There is at least moderate evidence consistently supporting air pollution, aluminium, silicon, selenium, pesticides, vitamin D, and electromagnetic fields as putative environmental risk factors for dementia. More and better research is needed and we suggest that this shortlist should form the initial focus of attention.”

3. Page 3, Line 12: "There is now consensus...." check its accuracy.

OUR RESPONSE: We feel it is justifiable to claim that “there is now consensus that a substantial proportion of cases are potentially preventable.” Several publications, including the World Alzheimer Report 2014,[1] highlight multiple potentially modifiable risk factors for dementia or make projections of the effects of risk factor modification on the number of people affected.[2-6] For example, the “Blackfriars consensus on brain health and dementia” concluded that up to 20% of cases of dementia could be prevented through risk factor modification.[7] Another article even used the optimistic title “Dementia … can be prevented.”[8]
Reviewer 2

This is a valuable review for the environmental risk factors for dementia. The paper is well written in general. I would like to recommend it for publication.

OUR RESPONSE: We thank the reviewer for their positive comments.

However, I hope the authors could address the following minor issues to improve this study.

1. The background part needs to be extended. It seems necessary to highlight more about the role of environmental factors among the different types of risk factors.

OUR RESPONSE: We have enlarged the background including mention of the two previous review articles (as suggested below in point 7):

“There is evidence from studying geographical variation in dementia rates that environmental risk factors may also be important in the pathogenesis of dementia.[9-11] Two previous reviews have reported on environmental risk factors for Alzheimer’s disease: both concluded that aluminium in drinking water and electromagnetic fields were important and one also highlighted occupational exposure to solvents and pesticides.[12, 13] However, both these reviews focused on Alzheimer’s disease rather than all-cause dementia and neither of them used robust, systematic review methodology and so may not have covered all potentially important risk factors. Thus, we present the first comprehensive systematic review on environmental risk factors for dementia.”

2. Citations are needed for "we also included factors not included in the general list which we knew had been linked to dementia risk, such as trace elements" at Page 4, 14-19.

OUR RESPONSE: We have now added a citation to a systematic review of selenium as an example:

“We also included factors not included in the general list which we knew had been linked to dementia risk, such as trace elements (for example, selenium[14]).”
3. More clarifications are needed for the statement, "however, if a review reported multiple new studies, we included the review as a single source of evidence" at Page 5, 9-13. Are you saying that you will use the review conclusion as the "single" evidence?

OUR RESPONSE: We have revised this sentence which now reads:

“However, if a review reported multiple new studies, we included the review as a single source of evidence, summarising its findings rather than including every study individually (e.g., Loef and Walach, 2012[15] included 101 individual studies).”

Including each study cited by such reviews individually for all the risk factors covered in the present review would not be feasible.

4. In Table 1, please consider moving down "Aluminium (occupational exposure)" to occupational exposure, or moving up "Lead (occupational exposure)" and "Metals (occupational exposure)" to "Other metals" The current classification seems not consistent.

OUR RESPONSE: We agree and have moved studies relating to occupational exposure to aluminium to the occupational exposure section.

5. Citations are needed for "one prospective study and the larger cross-sectional studies tend to support an association between aluminium and dementia risk" at Page 10, 34-39.

OUR RESPONSE: We have added these citations.

6. Give specific study information for "the fact that a number of exposures were only studied in a single study also weakens support for them as it is impossible to examine the consistency of the association in multiple studies" at Page 15, 33-39.

OUR RESPONSE: This information is available in Table 1. Rather than list each risk factor for which only one study was found, we now refer the reader to Table 1:
“The fact that a number of exposures were only studied in a single study (see Table 1) also weakens support for them as it is impossible to examine the consistency of the association in multiple studies.”

7. I suggest mentioning and introducing about the two previous reviews at "Comparison with previous literature" at the background, and then revisiting these two papers at the conclusion.

OUR RESPONSE: We have done so, as outlined above in response to point 1.

REFERENCES


