Author's response to reviews

Title: Rationale, design and methods for a community-based study of clustering and cumulative effects of chronic disease processes and their effects on ageing: The Busselton Healthy Ageing Study

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Author's response to reviews: see over
Dear Editor,

We submit our revised manuscript titled, Rationale, design and methods for a community-based study of clustering and cumulative effects of chronic disease processes and their effects on ageing: The Busselton Healthy Ageing Study for publication.

Below are the detailed responses to the reviewer’s suggestions and questions.

Yours Sincerely

Alan James

Chairman, Steering Committee
Busselton Healthy Ageing Study.

Point by Point Response to Reviewers.

Reviewer: Gerhard Schön

Reviewer’s report:

Major Compulsory Revisions

1. Section 'Data Analysis and Statistical Power', subsection 'Estimation of the prevalence of multiple chronic disease processes': "... will allow the prevalence in each group to be estimated with standard error of 3% to 4% and much more accurately ...". A standard error has no unit, so 3% to 4% makes no sense. A sensible measure of precision would be a confidence interval. But the size of the confidence interval changes at given sample size with the size of prevalence. Some examples for expected prevalences and its confidence intervals would be helpful.

The reviewer’s points are taken and the appropriate changes and examples are included – Page 21, Paragraph 1

Minor Essential Revisions

1. Section 'METHODS', subsection 'Study sample and recruitment process.': "Study enrolment is randomized". There is in fact little randomness in the sampling. The electoral roll says, that there are 6,690 adults eligible to participate. If we take into account none-response and refusal to participate, the study is more like a census survey than a randomized trial.

The randomness refers to the order of contacting the potential participants. This is clarified on Page 10, “Methods”, Line 6.

2. I have concerns that the study region is not representative. The homepage (http://www.busseltonhealthstudy.com/index.html) says, that the "residents of the town of Busselton, have been involved in a series of health surveys since 1966". It is likely, that the population of that
region shows larger health-conscious behavior, than on average. Due to the fact that clinically relevant results are provided to all participants, healthcare utilization will increase. The authors should comment on representativeness of the study.

Representativeness is discussed in a new section outlining the Limitations of the Study, Page 25.

3. Section 'DISCUSSION'.
"Finally, the BHAS provides feedback to each participant on clinically relevant outcomes (see Tables 1 and 2) with advice to take results to their usual medical practitioner." This is a desirable result from an ethical point of view, but the authors should expose the possibility of biased results. Every inquiry can be considered as an intervention, which may influence the results of longitudinal analyses.

The potential bias introduced by intervention inherent in the longitudinal study is addressed in Limitations of the Study, Page 25.

Reviewer: Emily Banks

Reviewer's report:

Minor Essential Revisions
1. It is best to avoid the general use of the term "interaction" in papers of this kind, unless describing statistical interaction (or effect modification), to avoid confusion.

The term “interaction” has been removed as suggested.

2. It seems logical that power for the cross sectional analyses would vary according to the prevalence of the specific condition, but this doesn't seem to have been mentioned. Could the authors please clarify?

The relation between prevalence and power has been included, Page 21, Paragraph 1.

3. On pages 22 and 23, the authors describe the main things the study will add. Since these are from cross-sectional analyses, particularly of prevalent disease, it is neither possible nor appropriate to assess causality, so it would be better if the authors could remove words that assume causality. For example, in point 2, removing words like "effect" and "reducing".

Assumptions of causality have been removed as suggested.

4. It is unclear why data from this local community would be generalisable to the whole country (point 1). This requires better justification.

The limitations of generalisability have been addressed in Point 1 and in a new section - Limitations of the Study, Page 25.
5. The discussion in general could do with a bit of toning down. For example, I suggest removing the word "uniquely" from point 3 - many other studies have gathered data on biomarkers and stored these types of samples. Ditto with words like "invaluable".

Unjustified hyperbole has been removed as suggested.

6. Please add a paragraph on the likely limitations of the study, including the limitations of the initial cross-sectional analyses, the relatively small sample size, especially for looking at effect modification, the local setting and population homogeneity.

A new section - Limitations of the Study, has been added on Page25.