Reviewer's report

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

Version: 2 Date: 5 April 2013

Reviewer: Emily Banks

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The submitted paper describes the protocol for a cohort study of 4,000 individuals from a community in Busselton, Western Australia. Detailed measures of a range of health related factors will be taken and cross-sectional and, ultimately, longitudinal investigations of healthy ageing will be conducted.

The article is well written and describes the study in good detail. I have a number of revisions to suggest.

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.

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?

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".

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

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".

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.

Level of interest: An article whose findings are important to those with closely related research interests
Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.