Author's response to reviews

Title: Examining the influence of gender, education, social class and birth cohort on cognitive tracking over time: a population-based prospective cohort study

Authors:

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Author's response to reviews: see over
Reviewer's report

Title: Examining the influence of gender, education, social class and birth cohort on cognitive tracking over time: a population-based prospective cohort study

Version: 2 Date: 28 May 2012

Reviewer: Kaarin Anstey

Reviewer's report:

The statistical analyses are thorough and sophisticated, and the major strength of the manuscript. The figures are excellent. The evaluation of cohort effects is extremely important and the authors raise methodological issues relating to this topic. The authors have also considered causes of dropout and included these in the statistical models. The paper makes a important contribution by demonstrating more broadly to the other groups how to approach these types of analyses which will become increasingly important in the future. The limitations all relate to substantive rather than methodological or statistical issues.

Major Compulsory revisions

1. The authors have only one measure of cognition and this is a dementia screening instrument that was not designed to measure cognition in the normal population. As the MMSE has ceiling effects in healthy older adults, it is particularly limited as a measure of cognitive change because it is unable to detect reliable change in those who are high functioning. This is the major limitation of the paper. Hence I think the title should be changed to refer to the MMSE rather than cognition, and likewise the abstract and results etc need to refer to change in the MMSE rather than cognition. The overall findings of the study need to be tempered due to this consideration.

Response to comment: We have changed ‘cognition’ to ‘MMSE’ throughout the paper. In the discussion (Page 9, paragraph 2) we now comment on the limitations of using the MMSE as a measure of cognitive function.

2. The introduction is relatively brief and makes strong generalizations about the findings on education and cognitive decline without surveying the literature in any depth or demonstrating knowledge of some of the key contextual factors that influence this relationship. The discussion is also very brief and does not raise many of the issues important for drawing conclusions in this field. The authors only cite one paper on education and cognitive decline in late life in the introduction, whilst there have been many papers published on this topic, (or that report the relationship of education to cognitive decline whilst focussing on other covariates). An evaluation of the literature on the association between education
and cognitive decline must consider the measures of cognitive function that have been examined longitudinally, and the measure of education. Measures of verbal ability are strongly associated with educational level, whereas measures of processing speed are less strongly associated with education. Hence education may influence cognitive change in these measures differently. It is well established that adults with higher levels of education perform better on the MMSE. These issues need to be elucidated to enable a balanced and informed interpretation of results.

Response to comment: We accept this point and have increased the literature review in the introduction (Page 3, Introduction, Paragraphs 2 and 3). We have also commented on the limitations of our measure of education and its relationship with the MMSE in the discussion (Page 9, paragraphs 2 and 3).

3. In the introduction the authors state that variation in study design may explain different findings for educational effects on cognitive decline. Another issue not mentioned by the authors is the measure of education used in these studies which may not be comparable between studies within and between countries. Most measures of education are quantitative and few rate the quality of education received. This may be as important or more important than study design.

Response to comment: We have added text to the introduction (page 3, paragraph 3) to address the issues raised by the reviewer.

“There may also be measurement and cohort differences for the effects of education on cognition. However, a recent publication from the 10/66 Study team showed increased education to reduce the risk of dementia across six middle-income countries.”

4. The use of a binary measure of education limits the sensitivity of the analyses of the effects of education. Given this is a focus of the current paper, this needs to be acknowledged as a major limitation in the discussion, or preferably, replaced with a continuous ordinal measure in the analyses.

Response to comment: We have now noted this in the limitations section of the discussion (page 9, paragraph 3).

“Another limitation may be the inclusion of education as a binary variable (less than statutory versus statutory or more). Whether years of education, highest qualification obtained, actual school grades, or a composite measure would be more effective is unclear and beyond the scope of the current analysis.”
5. I do not think that many would agree that ‘cognitive norms’ (page 4) can be derived from this instrument. I suggest that “MMSE Norms” would be more appropriate and less open to criticism.

   **Response to comment:** We have made the suggested change.

6. A **limitations** section needs to be added to the discussion. This needs to include discussion of the limitations of the MMSE for measuring cognitive change in healthy adults, the lack of measures of the major cognitive abilities, the known association of demographic factors with MMSE performance and the limitations of the education measure.

   **Response to comment:** A limitations section has been added to address these points (page 9, paragraphs 2 and 3).
Reviewer's report

Title: Examining the influence of gender, education, social class and birth cohort on cognitive tracking over time: a population-based prospective cohort study

Version: 2  Date: 5 June 2012

Reviewer: Darren M Lipnicki

Reviewer's report:

This short manuscript reports on how longitudinal change in MMSE scores in older individuals is affected by gender, education, social class, birth cohort and region of residence. The study addresses effects that are likely to be of interest to others, but there are issues I believe make the manuscript unsuitable for publication in its current form. My major concerns relate to how the methodology is described and a need for the authors to more clearly outline the implications of their study.

Major compulsory revisions:

1. MMSE scores are presented for a 1923-7 birth cohort up to the age of 95. Paragraph 2 of the Discussion and Conclusions section notes that “cohort effects were extrapolated across the age range”. This aspect of the methodology should be more clearly outlined in the Methods section, and the extent to which the conclusions are based on simulated or extrapolated data should be addressed.

   **Response to comment:** We have added the following sentence to the discussion (page 8, discussion, paragraph 2) to explain the extrapolation that was used to calculate the old-age scores for the youngest cohort.

   “This means that due to there only being 10 years of follow-up, the trajectories of the youngest cohort at the oldest ages were based on the results from the older birth cohorts who were observed at those ages during the study.”

2. The statistical analyses used are described very briefly, and I am unsure as to whether there is sufficient explanation given to fully describe them or allow for replication.

   **Response to comment:** We have re-written a large part of this section to provide a more detailed description of our analysis.

   “A detailed description of the analysis methodology has been reported previously [22-23]. Briefly, the methods account for all of the longitudinal data and adjustments are made for individuals who have missing
information using inverse probability weighting. Individuals are initially regressed against missing the next longitudinal data point based on their age, sex, centre, living alone, education, study route to interview and MMSE seen at the last non-missing interview. The model is then expanded to estimate a regression coefficient for their missing MMSE score which has the effect of removing the need for the prior regression coefficient for MMSE from the model (when the coefficient in the logistic regression equals zero). The predicted probabilities from this model are then used to define the inverse probability weights. These weights are then combined with a generalisation weight back to the original population to create a complete weight per individual per interview.

These weights are then used within a standard cubic spline regression model with knots at ages 70, 75, 80, and 85.”

3. Reasons for including social class in the analysis are not provided in the Introduction.

Response to comment: We have added the text and references to introduce the association between social class and cognition in the introduction (page 3, paragraph 2).

“Systematic reviews and individual studies have linked cognitive reserve factors such as education, occupation and social class, and social engagement to a decreased risk of dementia and cognitive decline in later life.”

4. The manuscript would benefit greatly by a more clearly apparent overarching rationale or message that follows through from the Introduction to the Discussion and Conclusions section. Are these particular effects being investigated to try and account for inconsistencies in the literature, or are there other theoretical and/or practical (or even clinically relevant) reasons?

5. The Discussion and Conclusions section seems more descriptive than interpretive. What are the implications of the findings?

Response to comments 4 and 5: The motivation for this analysis was to look at cognitive performance at a whole population level to see whether there are major influences that researchers need to be aware of. We have made alterations to the introduction and discussion to address the points made by the reviewer. In particular, we have reworked the final paragraph of the introduction and the penultimate paragraph of the discussion.

“In the absence of cohort effects, population norms based on cross-sectional data could be used to describe population average scores. However, taking norms from cross-sectional data fails to utilise all of the
information available from population-based longitudinal studies. This analysis employs methods that overcome these issues and calculates norms based on the complete data resource."

“Moreover, the calculation of population norms is often restricted to cross-sectional (baseline) data without utilising information from all available longitudinal follow-up waves.”

6. The last paragraph of the Discussion states that “Alternative study designs are needed to provide definitive conclusions about cohort effects.” Do the authors have suggestions as to more appropriate designs, and is the use of extrapolated data a significant limitation of the current study?

Response to comment: In our analysis we show that even in the presence of missing data and a complex study design, there are sophisticated methods that can be used to examine cohort effects. However, as we note in the second paragraph of the discussion, the gold standard data to analyse such trends comes from studies like the Seattle Longitudinal Study where there is a combination of static and dynamic cohort designs.

7. I think the authors should discuss the extent to which the effects investigated are independent of one another, and whether relationships between these influenced the findings. To what extent do the effects of education and social class/occupation overlap? Are centre effects influenced by education or social class?

Response to comment: The question as to whether these factors are independent is certainly an interesting one. However, the extent to which this can be investigated within the present analysis is currently limited by the methodology required to generate the estimate and the confidence interval (spline regression within a single category and then bootstrap simulation to obtain the error).

8. Paragraph 1 of the Methods section ends with “Written informed consent for participation in the study was obtained from participants or next of kin.” This leaves me wondering under what circumstances and in how many cases next of kin provided consent. It would also be appropriate to outline the exclusion/inclusion criteria for participation.

Response to comment: We have changed this sentence by removing “or next of kin”. While a close relative was able to provide consent and subsequently an informant assessment of the participant’s general condition, all cognitive tests were completed by the participants and this required participant consent.
Minor essential revisions:

9. Some attention needs to be paid to punctuation, particularly a lack of commas. There are also a few other language issues that I am sure would be picked up with further proofreading, e.g., the last sentence of paragraph 2 of the Methods currently reads “Self-reported education were split into...”.

**Response to comment:** We have made the suggested changes and have also re-read the manuscript and corrected any additional errors.