Author's response to reviews

Title: All-cause mortality in the Aberdeen 1921 birth cohort: effects of socio-demographic, physical and cognitive factors

Authors:

John M Starr (jstarr@staffmail.ed.ac.uk)
Ian J Deary (I.Deary@ed.ac.uk)
Lawrence J Whalley (l.j.whalley@abdn.ac.uk)

Version: 2 Date: 13 June 2008

Author's response to reviews: see over
Reviewer 1

The main message of this manuscript is that men are more likely to die than women at older ages and may indicate slower biological ageing among women as the mortality differentials are not due to differentials in illness or cognitive function. There is a potentially interesting message here but I have concerns about the statistical methods used.

Major compulsory revisions
1 If I understand correctly, a sequence of models was run successively adding variables but the numbers in the model differed because of differing numbers with values for a variable. This means that any differences in parameters between models could result from a mixture of confounding and changes in the population base. Comparisons across models should only be made with the same individuals in each model. As UCO was only available for 82 individuals the base for the models with UCO were presumably smaller than this, considerably reducing ones power to detect risk factors.

My suggestion would be to create a parsimonious model with the variables for which at least 180 have values and then as a separate exercise (and all the modelling would have to be done afresh) creating one for the small number who also had the AVLT, BD, DS and UCO.

We understand the Reviewer's concerns, though these were not voiced by Reviewers 2 and 3. Essentially, the concerns only affect the models that include cognitive data, the final ones to be considered, since we took a stepped approach. If we were to treat participants who had AVLT, BD, DS and UCO separately, we would severely limit the breadth of cognitive data available in the cognitive models of the main analyses. Instead we have inserted a sentence regarding this issue in the limitations section of the Discussion.

2 There are conflicting statements. On page 7 the analysis section refers to â##entering those with least missing data firstâ## and on page 8 there is reference to backward elimination without specification of the criterion used for elimination. It can be legitimate to do both but clarification is needed.

We have now made this explicit. Missing data numbers were used to determine the model staging, backward elimination at p>.1 for each modeling stage.

3 Did all the health status and mental ability variables have a distribution sufficiently close to normal to include them in a hazard regression analysis as
continuous and untransformed?

Apart from those that were set as categorical variables, we considered the distributions of continuous variables not to be so skewed that they could not be entered as such into the regression models.

4 The multivariate results (p8) at present do not allow of a clear interpretation. If the final models only contained 80 people or fewer (although, admittedly more person years), did this subset have sufficient variation in some of the other variables like smoking or depression for there to be scope for a significant association with mortality? Although smokers’ mortality rates were statistically significantly higher than never-smokers they may have been unimportant in the modelling if they are a rare group and so been eliminated in fuller models 5 Potentially, there is an interesting message if the gender differences are not accounted for by a variety of other factors but I am not convinced that the sample size allows one to be sure of this.

Gender was consistently significant in all models. We considered smoking as an important predictor even though it was eliminated in the optimal cognitive model (see first paragraph of the Discussion). In the context of extensive previous evidence, we interpret our findings as supporting the effects of smoking found with the larger samples in the non-cognitive models, but not found due to type 2 statistical error in the cognitive models (as the Reviewer notes in point 1, above).

Minor essential revisions
1. Background p 3 para 1 last sentence. Suggest reword: â## .. beyond 75, so that fewer would be able to benefit from any protective effects of the higher IQs â## (It is not the protective effect of high IQ that would be less but the smaller numbers of those with high IQs meaning that the population impact of the protective effect is less).

This nuance is difficult to capture succinctly, so we have inserted the word ‘overall’ to clarify this.

2. Source of sample. It is not clear how the 354 people in the analysis came from. There were 234 at wave 1 and we are told that 47 were recruited at wave 2 and 16 at wave 3.

We have inserted the term ‘refreshment of sample’ to explain this.

3. Methods: Were the 5 with unknown vital status at the time of moving away excluded from the analyses?

Yes. We now state this.

4. Why was UCO was entered into the multivariate models if it was not
significantly associated at the univariate level â## did the authors anticipate negative confounding with age?

Not necessarily just age. In fact age 11 IQ is probably the most important ‘confounding’ variable for the cognitive variables since around 50% of variance in mental ability in old age is explained by childhood IQ. Hence it is necessary to examine all the cognitive variables in multivariate models (with age 11 IQ at the very least). Actually, because we had a narrow age cohort, age is less of a problem as a confounder than in most studies.

5. Results: What was the age range? They were all 75 or 76 in 1997 but were some older at the time of measurement (see q on sample above). How many person years were involved in the Cox proportional hazards models

The difference between minimum and maximum participant age was 1.87 years for Wave 2 (mean age 14 days less than median age), 2.10 years at Wave 3 (mean age 15 days more than median age), 1.69 years at Wave 4 (mean age 6 days more than median age) and 1.56 years (mean age 4 days more than median age) at Wave 5. Since the mean and median ages are very close, overall person years could be calculated from the data we provide. However, as the Reviewer points out, the sample size is different according to which analysis is being considered, so an overall figure is probably not very helpful.

6. Table 1 â## mean and sd inappropriate if the variables are skewed. The sd for alcohol is larger than the mean. No values given for blood pressure.

We now provide median and interquartile range for alcohol and have inserted the BP values that were inadvertently omitted.

7. Page 5 second line of measures. â##mentalâ## not â##metalâ##

We thank the Reviewer for pointing out this typographical error which we have corrected.

8. Page 5 line 10 â## is this first attendance in adulthood or first of the waves mentioned under sample .

As adults; we have now made this explicit.

9. The variables given in Table 1 do not match up with those in Table 2 (e.g. living alone and smoking not in Table 1 and the components of crowding but not the index itself)

We had inadvertently included alcohol as a Demographic or environmental variable in Table 1. We have now corrected this since it should accompany smoking as a health variable. Hence neither alcohol nor smoking appear in
Table 2. Table 1 presents directly observed variables. Crowding index is a calculated variable, hence its appearance in Table 2 but not Table 1.

Discretionary revisions
1. P3. The reasons for all-cause mortality had falling by less among the 75+ than among younger ages could include the cumulative insults we experience to our bodies over the lifetime.

This is possible, but since we have shortened the Introduction as recommended by Reviewers 2 and 3, we have no obvious place to list this possibility.

2. P9 para 2 reference 17 refers to a sample from one family practice â## was it definitely representative of the Dutch population?

The sample was not absolutely representative since it excluded a small number of individuals with dementia, cancer or in institutions. So we have softened this phrase because total representativeness is not the issue for the argument.

3. P11 second para could be more succinct. Could replace first three sentences by â##One advantage of a narrow and older age cohort is that key predictors of mortality can be considered as measures of biological age or a sign of the bodyâ##s vulnerability to death sooner rather than laterâ##

The reason we were less succinct (i.e. spelt this point out explicitly) was to make it really clear to readers who may be less familiar with these arguments favouring narrow age cohort studies than the Reviewer.

4. Conclusions: Suggest omitting the sentence about mortality being common beyond 76 years of age.

We could omit this sentence, but then sentence 2 would make a rather abrupt start to the Conclusion.

Page 10 last para. Some good points made about the limitations.

We thank the Reviewer for this positive comment.

Reviewer 2

The topic of the paper â##All-cause mortality in the Aberdeen 1921 birth cohortâ## is completely clear explicated in the title of the manuscript. The authors try to answer a question what characteristics of cohort members and in what degree influenced to their survival from age 76 to age 86.

It is significantly interesting that the authors have data characterized subjects at age 11. For answer to this questions authors applied standard statistical methods
and the SPSS 14.0. The methods are well described and as it is possible to understand from the paper they did it correctly. It seems to me that the description of the results is clear and objective (some of result is really unexpected) as well as the discussion.

From my point of view it is only one point that needs in principal revision. It is the first paragraph of the Background. The authors tried to describe trends of mortality in Scotland from 1980-82 to 2002-02 based on crude death rates (CDR). It is absolutely unacceptable because CDR first of all is a function of population age-sex structure. In all developed countries this period is characterized as a period of fast mortality decline in old ages unlike earlier periods when old age mortality declined very slowly or even grew. In case of Scotland it explains about 25% of all life expectancy growth from 1980-82 to 2002-02. More problematic situation was at ages 20-39 where male mortality increased. I am sure that this paragraph is not an essential part of the paper and recommend to the authors to replace it with some other introduction more corresponding to the main topics of the manuscript.

We are happy to omit the crude death rate data; as the Reviewer points out these are not essential to the paper. Instead we have cited a previous study of all-cause mortality in the UK.

Reviewer 3

This is an interesting and important study for the understanding of the effects of early life conditions on survival in old age. The sample is relatively small and some of the loss of 1921 cohort members is problematic for the generalization of the results but it is difficult to do much about it. It is also discussed by the authors. The strength is the 1932 measures.

Major Compulsory Revisions
1. The title is too broad and ought to be more specific

We have extended the title to make it more specific.

2. The introduction is too much on mortality in general. It is to some extent a kind of prediscussion of the results. Both the introduction and discussion need to incorporate the vast literature on terminal decline on cognitive functioning, pulmonary functioning and health in general. As is now the article does not relate to earlier important research. There are for example several articles in Journal of Gerontology, The Handbook of Psychology of Aging, 4th edition, and also several review articles in other journals. If it relates better to earlier research it will be a much more important addition to the knowledge about factors behind survival in late life.
We are happy to accept the suggestions of the Reviewer and cite a previous mortality research that included a wide range of health, lifestyle and cognitive variables to provide the reader with a useful background to the study.

Minor essential revisions
3. *It would be good if a little more could be added on the ABC1921 study both in 1921 and at the follow-up*

We are unsure what the Reviewer requires here. There was no study in 1921; this was the year of the participants’ birth. The original 1932 study is described in detail with further references. We provide the dates of all five waves of follow-up together with details of the data collected.

4. *It would be good if a little more about the Moray House Test. What cognitive factors does it measure?*

We have added a brief description in the Methods section together with re-citing reference 10 that provides full details.