Research Editor
The BMJ

28th of June, 2021

Dear Dr. Islam,

BMJ-2021-065492 entitled "Terminal decline in objective and self-reported measures of motor function over 10-years before death: results from the Whitehall II cohort study"

Thank you. Please see below our detailed response to suggestions from the editorial board. The response has been itemized and includes the suggestions, our response, and changes made to the manuscript (included in the response letter as text in boxes).

We hope that the revised version of our paper has addressed the concerns raised and is now suitable for publication.

We would like to thank you for considering our paper and look forward to hearing from you.

Yours sincerely,

Benjamin Landré, on behalf of all authors

Editor's Comments

1.The findings are often described as "associated" with an outcome. Based on how a motor function was defined, HRs were 1, indicating a lower and higher risk of mortality associated with the motor functions, respectively. Therefore, it it very important to describe the direction of the association with a qualitative description ((whether any motor function is associated with a higher or lower risk of mortality). Please clarify this throughout the manuscript.

OUR RESPONSE: We agree with the editors and have modified the description of the findings throughout the manuscript to allow clear interpretation of the results. Please see our response to the all other comments below.

2.To this note, in the results section (p12), the HR for walking speed was 1 in the last paragraph (because the exposure variable was defined as a 'decline in walking speed'. Might you consider re-defining all the motor functions such that the HRs are in one direction (e.g., >1) for all the variables (for example, by reversing some of the motor function definitions). This should be accompanied by a clearer description of the exposure and outcome (for example, a decline in grip strength, or a decline in walking speed etc. was associated with a XX% higher risk of mortality (HR: 1.XX, 95% CI: pp to qq).

OUR RESPONSE: Thank you for your suggestion. We have revised the analyses and presentation of results so that all HRs represent poorer motor function performance (Table 2) or decline in motor function over time (eTable 6). To do so, we have reversed the scores of the walking speed, grip strength, and self-reported physical component summary scales as per your advices. We have also reformulated sentences to improve interpretation of the findings. See an example below:

Results, page 12 to 13, line 275 to 278

The associations were stronger when follow-up was shorter, for example one SD slower walking speed was associated with a 22% (HR=1.22; 95% confidence interval, 1.12 to 1.33) higher risk of mortality when assessed in 2007-2009 and a 49% (HR=1.49; 1.24 to 1.79) higher risk when assessed in 2015-2016.

3. Please add the interpretation of the HRs in the results (including in the abstract), rather than just copying the HRs from the Table (please see the example in the point above).

OUR RESPONSE: Thank you, we followed this advice and have reformulated the results including in the abstract as also suggested in comment #2. See extract from the abstract below:

Abstract, page 2, line 41 to 44

One sex-specific standard deviation poorer motor function in 2007-2009 (N cases/N total=610/5,645), was associated with an increased mortality risk of 22% (hazard ratio 1.22, 95% Confidence Interval 1.12 to 1.33) for walking speed, 15% (1.15, 1.06 to 1.25) for grip strength, 14% (1.14, 1.07 to 1.23) for timed chair rises, and 17% for PCS (1.17, 1.08 to 1.26) over a mean 10.6-year follow-up.

4. The unit of the motor functions is missing from the interpretation. Therefore, it is not immediately clear how to interpret these findings. The results are currently presented as, for example, walking speed was associated with mortality. It is missing most of the important aspects of the findings. It should be described in terms of both the unit of the exposure (e.g., one SD, equivalent to YY cm/s, increase, or decrease, in walking speed was associated with a xx% higher or lower risk of mortality over tt months or years, if applicable).

OUR RESPONSE: Thank you. We have added the unit of each motor function measure in the results section and in footnotes of the table and figure to ease interpretation of the findings.

Results, page 12, line 265 to 267

Sex-specific SDs correspond to a difference at baseline of 26.2 and 25.4 cm/s in walking speed, 8.5 and 6.2 kg in grip strength, 3.3 and 3.6 seconds in timed chair rises, and 8.0 and 10.7 in PCS score among men and women respectively.

Results, page 12 to 13, line 275 to 278

The associations were stronger when follow-up was shorter, for example one SD slower walking speed was associated with a 22% (HR=1.22; 95% confidence interval, 1.12 to 1.33) higher risk of mortality when assessed in 2007-2009 and a 49% (HR=1.49; 1.24 to 1.79) higher risk when assessed in 2015-2016.

5. To this, the wording for "timed 5 chair-rises" is still a bit dry. Could you consider writing it in plane language, such as, an additional XX seconds (which is equivalent to 1 SD) needed to raise five chairs were associated with ....

OUR RESPONSE: We have replaced the name of the test by “timed chair rises” and added information on the interpretation of results.

Results, page 14, line 311 to 313

Survivors had better performance than decedents on timed chair rises starting at year 10 (0.35 (0.12 to 0.59) SD; equivalent to a difference of 1.2 (men) and 1.3 (women) seconds), and this difference increased steadily with approach to time 0 (0.81 (0.61 to 1.02) SD; corresponding to 2.7 (men) and 2.9 (women) seconds).

6. Please remove p-values from the Results section, except probably the first paragraph of the "Time to event analysis subsection". Please also replace the p-values with the estimates and their 95% CIs in the abstract.

OUR RESPONSE: Thank you, the p-values have been removed from the manuscript, except from the suggested paragraph. They have been replaced by estimates (+ 95%CIs).

Results, page 14, line 308 to 318

The shape of the overall 10-year trajectory of walking speed and grip strength (Figure 1 and Table 3) was similar in survivors and decedents.

Survivors had better performance than decedents on timed chair rises starting at year 10 (0.35 (0.12 to 0.59) SD; equivalent to a difference of 1.2 (men) and 1.3 (women) seconds), and this difference increased steadily with approach to time 0 (0.81 (0.61 to 1.02) SD; corresponding to 2.7 (men) and 2.9 (women) seconds). The PCS score was higher in survivors, indicating better motor function, starting from year 7 (0.15 (0.05 to 0.25) SD; 1.2 (men) and 1.6 (women) score difference) and this difference increased over the period to time 0 (0.51 (0.31 to 0.70) SD; 4.1 (men) and 5.5 (women) score difference). The probability of IADL/ADL limitation was lower in survivors started from year 4 (0.02 (0.00 to 0.04)) with an increasing divergence to year 0 (0.09 (0.2 to 0.16)).

7. Table 2: if all the estimates had a p <= removed the *.

OUR RESPONSE: Thank you, revised as suggested.

8. Table 2: additional descriptions (such as "N mortality/N total = ...") are very important, but from visual perspectives, these would be better placed as Table legend/footnotes. Please consider moving them. Also, please describe them in the results section.

OUR RESPONSE: Thank you, revised as suggested.

9. Table 2: please add the unit of measurements for all the motor functions. Also, please add a note in the table saying that the HRs are for every one SD increase/decrease in the motor function along with the SD estimates for each of the motor functions (except Limitations in ADL/LADL?) This will allow easier interpretations, such as the HR is for every XX m/s change in the specific motor function. Please also add the estimates of SD in the results section.

OUR RESPONSE: Table 2 and supplementary tables are based on the same template have been modified following the editors' suggestions. The results section was also updated accordingly.

Results, page 12, lines 265 to 267

Sex-specific SDs correspond to a difference at baseline of 26.2 and 25.4 cm/s in walking speed, 8.5 and 6.2 kg in grip strength, 3.3 and 3.6 seconds in timed chair rises, and 8.0 and 10.7 in PCS score among men and women respectively

Table 2, page 28, lines 617 to 619:

* HRs for mortality associated with 1 SD sex-specific poorer motor function, corresponding to 26.2 (25.4) cm/s slower walking speed, 8.5 (6.2) kg lower grip strength, 3.3 (3.6) more seconds to undertake timed chair rises and 8.0 (10.7) lower score in PCS in men (women) respectively. Limitations in ADL or IADL reflects having 1 or more limitations.

Comments from the PPI Editor

1. The acknowledgment is clear and beautifully written. We need your dissemination plan and barriers to PPI. Participants are not the same as public involvement partners, they are people outside of the study that works with the research to complete the study. Please consider the Patient Reviewers comments in your revision.

OUR RESPONSE: Thank you, we have revised this section as follows:

Methods, page 6 to 7, lines 123 to 134

Participants of the Whitehall II study and members of the public were not involved in setting the research question or the outcome measures, nor were they involved in developing plans for recruitment, design, or implementation of the study. We recognize the importance of public involvement in instigating change in policy and practice but at the present time funding for these activities was not available. The principal investigators of the Whitehall II study are in the process of seeking solutions to strengthen this aspect of the study. The present analyses are part of a post-doctoral fellow's research where no funds were available to consult or involve the public. Therefore, participants and members of the public could not be asked to contribute to interpretation or writing up of results before submission. We are grateful to the patient reviewer who made insightful suggestions that contributed to better contextualize our findings in the discussion section.

All results are disseminated to study participants via newsletters and our website, which has a participant portal, https://www.ucl.ac.uk/epidemiology-health-care/research/epidemiology-and-public-health/research/whitehall-ii/participants-area and to a larger audience via media outreach.

2. PPI: Please add the reason(s) for not involving members of the public in your own words (e.g.) funding or training restrictions, access to software, COVID etc, also it may be that speaking to patients inspired this review if this was the case it is fine to add that although there was no direct PPI in this paper due to ____we did speak to patients about the study and we asked a member of the public to read our manuscript after submission. Please place the PPI declaration at the end of the methods.

OUR RESPONSE: As described above we have revised this section and acknowledge involvement the patient reviewer at the revision stage.

3. DISSEMINATION: This is mandatory and where you tell the readers how you plan to share your work. Ideas, distribute to clinicians and advocacy groups, use to run a trial where there will be PPI, use to inform good clinical practice by blog, press release, companion article written with a patient about the results. Social Media, plain-language summary on a web site etc.

OUR RESPONSE: Apologies, we have now included this section, please see below.

Page 21, line 466 to 468

Dissemination plan: The dissemination plan aims to target a wide audience, including members of the public, patients, and health professionals. It will be achieved using various channels: media outreach via press release from Inserm and University College London, scientific networks, and social media.