Author's response to reviews

Title: Age, gender and disability predict future disability in the elderly: the Rotterdam Study

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Author's response to reviews: see over
Dear editor and reviewers,

We like to thank the reviewers for their thorough reading and useful comments on this manuscript. We think the manuscript improved by incorporation of the comments and suggestions. We revised the manuscript according to the amendments suggested by the editor and reviewers as follows (reviewers’ comments are in italic).

Reviewer: Tatsuro Ishizaki

Major Compulsory Revisions
1. The results shown in this paper may be flawed by selection bias, because 37% of subjects (n = 2,956) who participated in the baseline survey were excluded in the multivariate analyses due to having missing data. The authors should explain any effect of the selection bias on the results in this paper.

   We thank the reviewer for pointing this out, and discussed this under limitations in the discussion section.

2. The authors should describe information on causes for disability (e.g., stroke, osteoarthritis, chronic heart failure, dementia, etc.). Without this information, it is difficult for readers to interpret the results appeared in the paper.

   Disability is a multifactorial problem and in this paper we evaluated predictors of disability in a multifactorial design. In risk prediction studies like ours, individual characteristics are combined in order to predict future disability in individuals. Risk models aim to identify “the risk of disability” and not “the cause of disability”. For evaluating the causes of disability we should have performed a multivariate analysis in which a causal relationship of one specific risk factor and outcome exists, adjusted for potential confounders. We did not choose to perform such an analysis. Nevertheless we discussed the matter more thoroughly in the discussion section.

Minor Essential Revisions
1. In Table 2, the authors would describe what kind of statistical model they used and what the reference category in the model was.

   The kind of statistical model used (polytomous logistic regression analysis) and reference category (the ‘no disability’ category being the reference category) were stated in the text. We choose to mention the reference category again in the legend of the table.

Discretionary Revisions
1. Because the authors mentioned about improvement in disability during the follow-up period in their paper, they would show a table that depicted transitions in functional status between the baseline survey and the follow-up survey.

   We agree with the reviewers and added a table showing transitions (see table 2).

Reviewer: Ching-Yi Wang

Introduction
1. The question posed by the authors is well defined. Just one recommendation, could the authors elucidate the differences between the predictor and the prognostic factors or the advantages of using one another? (Discretionary Revisions).

   We thank the reviewer for pointing this out. We chose to use the word predictor as we evaluated risk factors as well as prognostic factors in one model. We clarified this issue in the introduction.

Method, Data Analysis
1. The predictors might be different for those whose disability status was “getting better”, “staging the same”, or “getting worse” between the baseline and six-year follow up and thus deserve to be examined separately. Could the authors also provide the proportion of people whose disability status...
was "getting better", "staging the same", or "getting worse" between the baseline and six-year follow up? (Minor Essential Revisions)

We agree with the reviewers and added a table showing transitions (see table 2).

2. Please add the rationale for including those whose disability status was "getting better" or "staging the same" in the data analysis for this study. (Minor Essential Revisions)

In most logistic regression analysis there are just two outcome categories: ‘staying the same’ or ‘worsening’. In this analysis we have more than two outcome categories, that is why we used a polychotomous logistic regression analysis otherwise we would lose a lot of information. We cannot think of any rationale to exclude people whose disability status is unchanged (‘staying the same’) or improved from the analysis, as these are logical outcome categories.

Results

1. In the last sentence of the second paragraph of “Predictors”, it said “The AUC of the basic...0.83, 0.67, 0.81, and 0.81,...0.85, 0.69, 0.82, and 0.83,..., respectively.” There were four AUCs reported. I thought there should be three AUCs for all pair-wised comparisons (between the “able” and all other three groups) for each the basic and extended model. The first AUC (0.83, 0.85) reported can not found in table 2 as well. Please clarify this. (Minor Essential Revisions)

In SPSS estimated response probabilities are calculated per outcome category and saved as new variables. The ROC-curves are then based on these estimated probabilities. The number of ROC-curves is determined by the number of outcome categories. Using a polychotomous logistic regression analysis with four outcome categories one gets four equations, one for each outcome category. The AUCs are calculated for each equation. Each equation provides the risk of getting the specific outcome. Because the ‘no disability’ is the reference category it is not included in the table, but an AUC can nevertheless be calculated as the risk of having ‘no disability’ after six years. The first AUCs are the AUCs for the reference category.

Discussion

1. The results of this study found that "age" and "prior disability" were the two strongest predictors of disability status at six years later. However, as the authors noted that age is not modifiable and prior disability can not guide intervention or prevention program. The modifiable predictors for those whose disability status was "getting worse" or "getting better", between all paired group conditions (no disable, mild disable, severe disable, and death), might be leading different intervention strategies for people at different stages of disability. May be for future studies? (Discretionary Revisions)

The reviewer states that ‘prior disability can not guide intervention or prevention program’, but this is not what we discussed in the discussion section. We stated that there is ‘an opportunity for preventing and treating disability’. Naturally there are various intervention strategies which appeared to be effective and indeed future studies could evaluate these interventions for people at different stages of disability.

2. Could the authors elucidate the advantages of including all participants with different disability status at baseline but rather than including those who were disability free only at baseline in this analysis? (Discretionary Revisions)

We thank the reviewer for this comment and discussed it in the discussion section under strengths and weaknesses:

“We wanted the model to predict future disability status in a general population of older people which comprises people with different functional status, those with and those without prior disability. Furthermore prior disability has shown to be a determinant of subsequent transitions with respect to functional status. We therefore wanted to study how significant this determinant would prove in our prediction model.”

Reviewer: Catherine Sherrington

Major compulsory revisions

1. The “what this study adds” section states that the model is to predict an increase in disability but this does not seem to be the case. The outcome seems to be disability per se rather than increased disability.
We thank the reviewer for this comment. We intended to state that the model is to predict disability and worsening of disability (people transferring to another outcome category). We deleted the word 'increase'.

2. The term "the elderly" should be avoided as many find this offensive. "Older people" or "seniors" or "people over the age of x years" should be used instead. This is particularly important as the sample includes those over the age of 55.
   We agree and changed it throughout the manuscript.

3. The introduction would be benefit from a better justification for the study. Prediction of disability is suggested to be useful for the identification of high risk groups for intervention yet the interventions quoted as examples are all in particular clinical groups rather than at a population level. The best way to target these interventions would seem to be to seek people with this diagnosis rather than screen the general population of people over 55.
   Indeed there are studies on interventions at a population level; therefore we added this to the introduction. Knowing that prior disability status is a major determinant of future disability one could screen the population for already existing (subtle) disability as even in those with disability their true functional status may not be evident for others at the first glance.

4. In the analysis section the meaning of "predictors which in earlier regression models have proven to be significantly associated" is not clear and needs explanation. Also, which interaction terms were included?
   We thank the reviewer for pointing this out and changed the sentence to clarify what we meant in the method section.
   After evaluating interaction of 'disability index' with different variables we found there was interaction between the variables 'disability index' and 'joint complaints'. We included this relation as an interaction term in our model as a product of both variables. This is added in the result section.

5. I would be interested to see the number of people in each of the outcome categories at baseline (currently this is just presented as the average score). This seems a way of assessing the extent of worsening of disability over time and could help the reader assess the additional information provided by the prediction model.
   We agree with the reviewers and added a table showing transitions (see table 2).

6. In the results, predictors section the attempt to assist the reader in interpreting the odds ratio is a good idea but I feel the wording needs more work as "An OR on a continuous variable, like the Disability Index, should be interpreted that with every point increase on the Disability Index the risk increases with that OR" does not seem quite right.
   We rephrased the sentence. We hope this is a better explanation.

7. The most recent International Classification of Functioning, Disability and Health from the World Health Organisation uses the term disability more broadly than the way it is used in this study. I suggest that this be addressed in the discussion.
   We thank the reviewer for this comment and discussed the differences in disability definition in the discussion section.

8. In Table 3, why is there a "+" after the constant in the "severe disability" column.
   Apologies, this is a typing error.

9. I suggest the footnote on Tables 3 and 4 be modified to give a clearer explanation to the reader on how the probabilities could be calculated in practice. Perhaps along the lines of the "The probability of each outcome for an individual can be estimated by adding the scores for each characteristic. The sumscore represents the predicted probability of each outcome category".
   We thank the reviewer for the suggestion for rephrasing the footnote. We changed the footnote using the suggestion of the reviewer.