Author's response to reviews

Title: Life style and longevity among initially healthy middle-aged men: prospective cohort study

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Version: 3 Date: 5 February 2013

Author's response to reviews: see over
Dear Editor.

Thank you for the high quality reviews and for the opportunity to resubmit our manuscript. We appreciate the suggestions from the reviewers, and we have attempted to revise the manuscript along the lines suggested.

We have updated our ethics statement to include the name of the ethics committee that approved your study.

In the following we have inserted our answers to the reviewers’ comments in blue.

Referee 1: Jamie Seabrook

Minor Essential Revisions
- need a comma in the Results section of the Abstract between "weight" and "55.4%"
- Under "Subjects," the second line states...."considered to be representative for the healthy working male...". Replace the word "for" with "of".
- Under "Subjects," it states that "Apparently healthy men, aged 40 to 60 years, were recruited..." Why "apparently"? That sounds unsure.
- Under "Subjects," paragraph 2, you need a comma after "Statistics Norway"
- At the end of the 2nd paragraph of the "Subjects" section, the authors give a mean of 55.3 years. What is the standard deviation? This measure of dispersion should always accompany a mean.
- Under "Results", capitalize all Table identification (e.g., Table 1, Table 2, not table 1, table 2).
- You need to describe Table 1 in the Results section. It sort of falls off a cliff in the text. Also, why no p values in Table 1?
- You need a coma after "non-smokers" and "normal weight" in paragraph 3 of the Results section. Also replace "men with overweight" with "men who were overweight" in that same paragraph. Lastly, your BMI categorization is incorrect in that paragraph. It states a BMI between 25 and 30 but Tables 3 and 4 use a categorization between 25 and 29.9 and >= 30.
- Capitalize "Figure" (not "figure") in the Results section.
- Discussion section, paragraph 2, should say "non-smokers" not "non-smoker".
- Paragraph 3, should say "grip-strength" not "grip-strenght". Also, it should state, ...."as the number of participants" not "as number of participants".
- Paragraph 6 of the Discussion should say, "and changed their smoking habits" not "changed their smoking habits..."

We have revised our manuscript, taking into account each of the above suggestions.

Major Essential Revisions
- Why is age being dichotomized into <55.6 years and >= 55.6 years? That doesn't make any sense.

We have changed cut-off for dichotomization of age to 55 years.

- All of the tables use "smokers" and "non-smokers" as the column variables. Is that ultimately what the authors are interested in showing? That smokers have a
higher risk of mortality controlling for some other lifestyle factors in initially healthy middle-aged men? If yes, that is not what I got from reading the Introduction and study's objectives (the latter which aren't clearly defined).

The discrepancy between result section and aim is now removed by rewriting the aim of the study. We have stated in the statistical section that statistical analysis was performed separately for smokers and non-smokers. The reason for presenting results for smokers and non-smokers separately is presented in the discussion section.

- In Figure 1, where is the legend for smokers vs. non-smokers? Without a legend for this variable, the bar chart is incomplete and confusing.

Figure 1 is removed in the revised manuscript due to comments from the other reviewer.

- The very last line of the Discussion section states, "Increased probability of longevity may be easier to understand for ordinary people than reduced mortality rates." I think you mean the general public?

*Ordinary people has been changed to general public.*

**Level of interest:** An article of limited interest  
**Quality of written English:** Not suitable for publication unless extensively edited  
**Statistical review:** Yes, and I have assessed the statistics in my report.

Referee 2: Aage Tverdal

Life style and longevity among initially healthy middle-aged men: prospective cohort study

It is of interest to study why some men live to advanced age. In this modest sized study population the focus was on life-style and survival to age 85 years.

Major  
The method is suboptimal. The framework is logistic regression with survival to 85 years (yes, no) as endpoint. Within this framework they had to exclude men who could not have attained 85 years at the end of follow-up. This exclusion (censoring) reduced the study population from 2014 to 821 (59%). A much more adequate framework is survival analysis. This study could estimate the survival between, say 45 years, and 85 years. Confer for instance the paper by R Sakata et al. Impact of smoking on mortality and life expectancy in Japanese smokers: a prospective cohort study. BMJ, 25 October 2012.

We agree that it would have been interesting to identify predictors of total mortality, using all the 2014 individuals. However, we aimed to examine possible predictors for the outcome reaching the age of 85 years. Thus we could not include individuals born later than December 31, 1921, because they could not have reached the age of 85 during the observation period.

We consider our aim to be markedly different from examining predictors of total mortality. Further, we wanted to be able to compare our results with a similar study published in JAMA (Willcox et al. JAMA 2006, 296:2343-2350), using logistic regression models to examine
possible predictors for the same outcome as in our study. For this reason we chose logistic regression models to analyse our data.

The huge selection of the study population makes it hard (impossible) to assess the validity of the findings. For instance it is found that (total?) cholesterol and systolic blood pressure have no significant impact on the chance of attaining 85 years. This should be compared with their previous paper (ref 3), where both these variables were significantly related to cardiovascular death which made up more than 50% of all deaths.

The 821 participants in our study were between 51 and 59 years old at baseline, and were only selected on the basis of birth date. Thus we consider the findings in our study to be valid for healthy Norwegian men between 51 and 59 years. As regards the lack of significant impact of cholesterol and systolic blood pressure, we have underlined in the discussion section that this lack of significance may be due to the relatively low number of participants.

Furthermore, if I understand table 4 right, smokers of more than 10 cigarettes (per day?) have a greater chance (odds) of attaining 85 years than smokers of less than 10 cigarettes? And is it more favourable to be obese than having a BMI below 25 kg/m2?

Table 4 presents the odds ratios of the probability of reaching the age of 85 years. Thus the odds ratio of 0.22 for non-smokers when comparing obese with having a BMI below 25 implies that it is unfavourable to be obese. Similarly, the odds ratio of 0.56 when comparing smokers of more than 10 cigarettes per day with those smoking less than 10 cigarettes implies that it is unfavourable to smoke more than 10 cigarettes per day. In table 4 we have replaced Cigarettes by Daily number of cigarettes, as suggested.

Minor
The recruitment took place during 1972-1975. The mortality rate has been steadily declining in Norway and I wonder whether date (or at least calendar year) of inclusion should be included in the models?

As suggested we have included calendar year at inclusion in our multivariable logistic regression models. Nearly identical results were obtained as those presented in the manuscript.

In the “Statistical Analysis” paragraph it is stated that: “The assumptions underlying multiple logistic regression analysis were checked and found to be adequately met”. This does not convey much information to the reader. What is checked and how was it done?

In the statistical section of the revised manuscript we have included a more detailed description of how we checked the assumptions underlying the multiple regression analysis.

In the discussion, paragraph 4, it is claimed that the interaction between overweight and physical fitness as predictors of longevity is novel. Where in the paper is this finding hidden and has there been done some statistical testing? There is nothing about interaction in the “Statistical Analysis” section.
The interaction between overweight and physical fitness among non-smokers has been tested had found not to be statistically significant. Thus figure 1 is deleted in the revised manuscript. Also the last paragraph in the result section is deleted, as well as comments about this interaction in the abstract and the discussion section.

The authors have rightly done analyses stratified by smoking status. It had been even better to study the never smokers as these person are likely to remain never smokers throughout the follow-up. Ex-smokers may start smoking again, and smokers may quit smoking. The smoking prevalence in Norway has been steadily declining throughout the follow-up period of this study.

We agree that it might have been better to study the never smokers, as these persons are likely to remain never smokers throughout the follow-up. However, in our study only 208 individuals were never smokers; hence we decided to keep our manuscript as it is on this issue.

**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.

**Declaration of competing interests:**
I declare that I have no competing interests