Author's response to reviews

Title: Late-life coronary heart disease mortality of Finnish war veterans in the TAMRISK study, a 28-year follow-up

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Author's response to reviews: see over
Enclosed please find a revised version of our manuscript entitled "Late-life coronary heart disease mortality of Finnish war veterans in the TAMRISK study, a 28-year follow-up" which we submitted to BMC Public Health (MS: 1839555755407991). The reviewers’ suggestions have been taken into account as closely as possible. Our specific comments are as follows:

**Reviewer**: Sidsel Graff-Iversen

**Reviewer's report**:
The topic of this study is important and this manuscript on late-life mortality in veterans is of public health interest. However, the information on the war injuries is very limited, the follow-up started decades after the war, and the number of men included is relatively low. Some major compulsory revisions need to be made.

First, it should be made very clear that the aim is to study late-life mortality in war veterans who were alive (and relatively healthy?) by the age of 55 years. This should be clear also in the abstract (Background).

We have added to the abstract (Background): We evaluated whether wounded Finnish World War II veterans who were alive at the age of 55 have increased long-term coronary heart disease (CHD) mortality.

We have also added to the end of the Background: We therefore wanted to pursue the hypothesis that wounded veterans who were alive at the age of 55 are more at long-term risk for coronary death than other veterans.

Next, physically wounded veterans are compared with war veterans who were not physically wounded. The two groups may have several mental and physical background differences, in addition to the difference in body height. The term ""control" should not be used here. Instead terms such as "comparison group" or "non-wounded veterans" can be applied.

We have replaced throughout the manuscript “controls” with “comparison group”.

A major limitation is that no information was collected from the physically wounded veterans on the nature/extend of the wounds/injuries, including possible longterm physical consequences. Table 1 tells something, but not very much, about their health at age 55. The veterans' high level of exercise may
imply that most of them did not have physical disabilities and that their health was fairly good. But it’s not clear if this was the case. Is it possible to extend Table 1 with more informations from the 1980 survey? Was a question on "health in general" included? Is there information on work or disability pension? Other measures on health and ability?

We have added such information to Table 1: Health in general % (good/average/poor); On disability pension % (yes vs. no).

In the methods: .. questions of vocation, possible disability pension and education. .. questions of health in general and mental health.

In the results we have added: Men who had been wounded or injured in action were taller and had slightly higher BMI, had more self-reported depression experienced during the last six months, and were more on disability pension, as compared with the comparison group at the age of 55.

In the discussion, a sentence has been added: The wounded men in our study had higher BMI and were more on disability pension, as compared with the comparison group. In addition to depression, also these factors could possibly be intermediary variables between trauma/stress and a CHD death.

Reviewer: Maria Inês Azambuja

Reviewer’s report:

1) The title suggests that the paper just wanted to establish if an association existed between being wounded in the war (1943-45) and dying from CHD after the age 55 (black-box approach). The conclusion, on the other hand, suggests that the true question was if an association could be postulated between traumatic events at early adulthood and CHD development late in life. To me the questions are not equivalent. Being wounded in the war may result in life-long physical disability, which would add additional potential CHD `risk factors´ (inactivity, obesity, depression, medications…) to the selected exposure: “early adulthood traumatic event”. On the other hand, traumatic events are not only physical. And if the hypothesis is one of association between stressful early-adulthood events and late CHD mortality, the exposed should possibly be all the military that were at the front (527) X men that were not (72+68).

Major Compulsory Revision – to clarify the study question

2) The study used a black-box approach. There was no attempt to model a causal hypothesis. This introduced some inconsistencies 1) regarding the question to be answered (see item 1); 2) regarding the modeling of the CHD mortality risk - would possibly be intermediary variables between trauma/stress and a CHD death (especially if chronic disability ensued). In this case, they should not be controlled for in the risk model (Major Compulsory Revision).

We have included only the unadjusted results in the Abstract (Results); we have removed:, when adjusted for BMI and depression.

We have also now discussed this possibility in the Discussion: The wounded men in our study had higher BMI and were more on disability pension, as compared with the
comparison group. In addition to depression, also these factors could possibly be intermediary variables between trauma/stress and a CHD death.

This study has undergone a previous review, where all three reviewers wanted depression and BMI to be controlled for in the risk model.

3) also, it seems to me that there is difference between previous reported CHD events (p=0.12) and diabetes (p=0.19) between the study groups – again, expectedly intermediate variables between early adulthood exposure (trauma/stress) and the outcome (CHD death).

Yes, but the differences are not statistically significant. However, the nonsignificant increase of previously reported CHD events in the wounded subjects in fact supports our finding.

3) The study population is small (compared to the studies referred by the authors), the choice of study groups is unconvincing if the underlying association to be investigated is one between stress and late CHD, and the variables are too loosely defined. Which criteria were used to classify exposed and “non-exposed” to trauma according to “smoking” for example, an important risk factor to CHD?

(Major Compulsory Revision)

Smoking was defined as current smoking. We have added to the Methods: Questions of health-related behaviour included current and past smoking. Also we have added to Table 1: Ever smoked % (yes vs. no). There was no statistical difference in this parameter between the wounded and comparison group. For the benefit of the reviewer, of the current smokers, 98% of those wounded and 92% of those in the comparison group had smoked for over 20 years.

4) Participation rate was 667/843. Does the Kaplan_Meyer curves - with significant losses in the exposed group in the first 1-2 years of the study followed by a recovery towards years 5-10 - suggest bias towards severely ill individuals during the recruiting of cases in 1980? Doesn’t that trend deserve a comment?

(Major Compulsory Revision)

We have added to the Results: There were significant losses in the group of wounded men in the first 1-2 years of the study followed by a recovery towards years 5-10. We have also added to the Discussion: It is notable that there were significant losses in the group of wounded men in the first 1-2 years of the study followed by a recovery towards years 5-10, which might suggest bias towards severely ill individuals during the recruiting of cases in 1980. However, this seems unlikely, since the final cohort included 79 % of all the 55-year-old men invited. On the other hand, we may not have seen the whole effect, since the present follow-up was started three decades after the traumatic experience.

5) Why the distribution of the main causes of deaths in each group was not presented? (role of competing causes of deaths) Discretionary Revision

This was also because of previous review.
6) Why the CHD deaths were not described according to year of occurrence? I believe that these descriptive data would add interest to the paper. Discretionary Revision, strongly recommended

We feel that these coronary deaths may be visualized from the Kaplan-Meier survival curve.

PS – Review the phrase “this study is an important contribution to the literature because most studies to date have looked at the effects of exposure to combat-related PTSD rather than exposure to combat itself” This is not the case here. Exposure was not to combat but to wound. (Major Compulsory Revision)

We have modified this sentence: this study is an important contribution to the literature because most studies to date have looked at the effects of exposure to combat-related PTSD rather than exposure to combat wound or injury.

We hope that these changes and additions will make the manuscript suitable for publication.

Sincerely yours,

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