Author’s response to reviews

Title: Cardiovascular Health and the Modifiable Burden of Incident Myocardial Infarction. The Tromso Study

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Author’s response to reviews: see over
Dear Editor-in-Chief

Thank you very much in deed, for allowing us to make improvements to our manuscript entitled “Cardiovascular health and the modifiable burden of incident myocardial infarction. The Tromsø Study”. We have revised the manuscript based on the minor comments from the reviewers. Please find enclosed the revised version of our manuscript. The details of our response to the comments from the reviewers are below.

Yours sincerely,

Tom Wilsgaard
Response to the reviewers’ report

Reviewer: Joshua Willey

Reviewer's report:

Minor essential revisions:
-the authors have addressed most of the comments. The primary comment on
the statistical interaction remains and the manuscript should emphasize that
differences between groups cannot be assessed. This is notable with the age
categories - that statistical interaction is likely to be multi-level which it is not clear
they have the statistical power for. If there is a multi-level interaction then model
fit with the equivalence of a likelihood ratio test would be needed.

Answer: In the reviewer’s first round of comments the reviewer asked us to assess the
interactions “AHA_index*gender, AHA_index*age”. We interpreted this as a suggestion to
assess whether our main effect size, the GIF, differed by age or by sex. Our action was to
include tests of differences between the mentioned groups. It is evident that that the reviewer
is thinking of other types of interactions.

We did not consider heterogeneity of the AHA_index effects by age and gender as an a priori
hypothesis since we have no substantive reasons to postulate such heterogeneity, nor do we
know of indications in the literature of such complex associations in this area. We therefore
tested the interactions mentioned in the previous paragraph. Although, GIF differences
between young and old were observed we did not assess higher-dimensional interactions. The
latter would challenge plausibility, be difficult to interpret if present, and could not be tested
with adequate statistical power, as indeed mentioned by the reviewer. Importantly, we do
present our results stratified by gender and by age, which alleviates potential concerns about
further heterogeneity of effects.

Reviewer: Delphine De Smedt

Reviewer's report:

Dear author,
Thank you for the revised version of your manuscript.
Please find herewith some minor issues.

Supplemental file 2: legend, numbering the cardiovascular risk factors is a bit
confusing, since you also use numbers for the Health metric score, maybe you
can use A, B, C etc.

Answer: Thank you for pointing this out. We agree and have changed the numbering to a), b),
c), etc. See table 2, table 3, and additional file 2.

Background line 66: to our knowledge, no study… There are studies that try to
assess the impact of lifestyle behaviour and medical treatment e.g. the IMPACT
study by Prof. Simon Capewell.

Answer: Thank you for pointing this out. We have included a study by Huffman MD, Capewell
S, et al. that aimed to evaluate recent trends in cardiovascular health metrics and to
determine whether the AHA 2020 goals will be met if current trends continue. Please see lines 296-300.

Discussion line 293: “reductions of magnitude between first two scenario’s have to be met”, is not clear. I still find the different scenario’s a bit to optimistic. What is change that those with health metric score #3 go to ideal levels. Maybe they improve on 1 risk factor (e.g. from 2 to 3).

Answer: We agree that without a population level intervention with focus on the “obesity epidemic” it might be hard to reach the goal of a 30% reduction in score levels < 4. This is further commented on as a result to the comment in the previous paragraph. Furthermore, among subjects with score levels < 4, 89% had a score level 3 (49%) or a score level 2 (40 %). A shift from low levels would therefore mean an improvement in only one or maybe two individual health metrics. The potential for individual improvement in this group is rather high as only 9%, 15%, 32%, 37%, 67%, and 97% had ideal levels in blood pressure, cholesterol, BMI, physical activity, smoking, and diabetes, respectively. Furthermore, our generalized impact fraction, GIF, does not include a scenario of a shift from score level 4 to score levels 5 or 6 (due to low power in the youngest age groups). Such a shift would result in a significant reduction on the hazard ratio of MI (see Table 2). Consequently, given a 30% shift in all score levels our GIF is likely underestimated.