

Author's response to reviews

Title: Estimating health-adjusted life expectancy conditional on risk factors: results for smoking and obesity

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Author's response to reviews: see over

Dear editors,

Herewith I submit the second revision of ‘Estimating health-adjusted life expectancy conditional on risk factors: results for smoking and obesity ’ including a detailed response to your concerns (see next pages). Most important revision of the paper is the addition of a sensitivity analyses with which we addressed also the other issues raised by you: the influence of trends in future disease epidemiology and the incomplete nature of the Dutch Burden of Disease Study. Results of the sensitivity analyses revealed that although HALE estimates are sensitive to changes in disease epidemiology differences in HALE between the different cohorts remain substantial. In a lot of cases, unhealthy life years were lowest for the ‘healthy living’ cohort and relative compression did not occur. However, in none of the scenarios relative expansion of morbidity occurred. This led us to nuance our conclusions somewhat with respect to the compression of morbidity. As a result, the abstract and discussion section have been altered also.

We hope you are willing to consider this revised manuscript for publication in Population Health Metrics and we look forward to hearing from you on this in due course.

Yours sincerely,
On behalf of all co-authors,

Pieter van Baal

Reply to remarks from editors

The original text from the editors is printed in normal face, while our reaction is printed in bold and italic

1. If RRs are used from cohort studies comparing risk in smokers vs never smokers (which the editors presume is what you used; the statement below is a bit ambiguous) it is not correct to apply these to population disease/mortality rates which are the combined impact of current smokers and ex-smokers; the correct way would have been to estimate current rates of mortality in smokers by taking out the excess risk (at the population level) that is contributed by ex-smokers using time since quitting and risk reversal info.

?For smoking, data from studies were used that reported relative risks for all former and all current smokers specified by gender and age.?

Apparently, we did not explain properly the methodology. To calculate baseline incidence rates we used the current distribution of smokers in three classes (never, current and former smokers) and relative risks for these three classes (age and sex specific) as explained in Appendix A. To calculate HALE for the cohort of smokers the baseline incidence rates are multiplied by the RR of current smokers only (not a mix of current and former smokers). Appropriate textual revisions have been made to explain this more clearly.

Ideally, when calculating the baseline incidence and mortality rates, former smokers should be stratified by time since cessation. However, data on this distribution is lacking in the Netherlands and not for all diseases included in the model relative risks since time cessation are available. Therefore, in the calculation of the baseline incidence rates relative risks of former smokers are not stratified by time since cessation. Of course, the validity of this assumption depends on to what extent the distribution of time since cessation in the Dutch population equals the distribution of time since cessation in the studies we used for our relative risks. However, since we focus on current smokers only in this paper relative risks of former smokers only enter the model in the initialization phase. Not including time dependent relative risk would not introduce major errors especially since relative risks are age specific and age correlates with average time since cessation. In general, we think that including time since cessation is more important when the aim is to estimate effects of smoking cessation interventions in which case the time since cessation is known in the intervention group and does not correlate necessarily that much with age anymore.

2. Conclusions about compression of morbidity in what is basically a multi-state period life table (i.e. assuming no trends in disease and death over time) should be made with great caution; uncertainty about future trends of course is great but a choice of assuming no such trends is probably a bigger error.

We agree that trends in disease and mortality are important. First of all, trends in disease prevalence and death, of course, occur due to the incidence prevalence mortality methodology used in the model. However, we did not estimate trends in incidence and death rates. As is also evident from the comments from Professor Manton, trends in incidence rates and death rates over time are very likely due to for instance changes in medical technology and care. To investigate the sensitivity of our results to trends in incidence and mortality rates we have included scenarios in a

sensitivity analysis in which mortality and/or incidence rates of all diseases in the model decrease over time (see response to comment 4).

3. As Dr Baarendragt points out the incomplete nature of disability estimates in the Dutch study could influence the conclusions about compression of morbidity considerably; as an alternative the authors could have used EURO-A prevalent YLD data from GBD or (if available) that specifically calculated for NL.

To address the incomplete nature of the Dutch study we investigated how sensitive the results are to changes in the age gradient of the health state valuations of the different cohorts. We have recalculated HALE estimates for all cohorts using GBD data to sharpen the decrease in HSV for all cohorts in the sensitivity analysis (see response to comment 4).

4. The editors would have expected an uncertainty analysis; given that this calculations are done in a simulation model that ought to be achievable.

For most parameters in the model probability distributions have not been estimated. Therefore, instead of an uncertainty analysis a sensitivity analysis has been added also addressing point 2, 3 and 5 by estimating HALE and LE for the three cohorts in the following scenarios:

- *scenario 1: a yearly decrease of 1% in attributable mortality rates for all diseases included in the model;*
- *scenario 2: a yearly decrease of 1% in disease incidence rates for all diseases included in the model;*
- *scenario 3: a yearly decrease of 1% in both disease incidence and attributable mortality rates for all diseases included in the model;*
- *scenario 4: a yearly decrease in all relative risks of the obese and smoking cohort using the following formula: $RR(t) = (RR(t-1) - 1) * 0.99 + 1$ where $RR(t)$ is the relative risk in year t ;*
- *scenario 5: health state valuations for all cohorts at all ages were recalculated by subtracting 30% of mean age and sex specific total disability (defined as 1 minus the health state valuation) as estimated using the Dutch Burden of Disease data. This implies a sharper decrease in the health status of the cohorts at older ages. At ages 80 and over this means a reduction larger than 0.1 in the health state valuations of all cohorts.*

In scenario 1, 2 and 3 the decrease in mortality and/or incidence rates roughly equals the decrease as used in the Global Burden of Disease projections of global mortality and burden of disease. Scenario 4 reflects the effects of selective disease prevention efforts in smokers and obese as has been observed in the past. In scenario 5 we account for the incomplete nature of the Dutch burden of disease: compared to the Global Burden of Disease 2000 study, the diseases selected in the Dutch Burden of Disease study account for only 70% of years lived with disability for European region A.

5. The first point raised by Professor Manton was meant to raise the issue that RR for BMI can change if some of the intermediate exposures (like diabetes and hypertension) are better treated over time. The current discussion around changes in distribution doesn't really address this paper. Two relevant related papers are:

Flegal KM, Graubard BI, Williamson DF, Gail MH (2005) Excess deaths associated with underweight, overweight, and obesity. JAMA 294:1868-1872

Gregg EW, Cheng YJ, Cadwell BL, Imperatore G, Williams DE, Flegal KM,

Narayan KM, Williamson DF (2005) Secular trends in cardiovascular disease risk factors according to body mass index in US adults. JAMA 294:1861-1867.

We interpreted the comment by Professor Manton as a critique on the all cause mortality risks used in the simulation model for the different BMI classes. Therefore, in the discussion section and in our previous reply we stressed the fact that the study Flegal is just one from the many studies addressing the relation between obesity, age and mortality. However, after reading the paper by Gregg et al. in JAMA we see that his comment also implies that future relative risks can change over time. Therefore, to investigate the sensitivity with respect to this issue we have included a scenario in the sensitivity analyses in which relative risks decrease over time (see response to comment 4).

6. Finally, the editors would like to ask you to clean up the paper's spreadsheet appendix (e.g. at the bottom of RR page some other terms like "knee" and "hip" appear which must have belonged to an older version of this spreadsheet).

The spreadsheet has been cleaned up!