Author’s response to reviews

Title: Socioeconomic inequalities in cardiovascular mortality and the role of childhood socioeconomic conditions and adulthood risk factors: a prospective cohort study with 17-years of follow up

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Author’s response to reviews: see over
To: BMC Public Health

Rotterdam, September 8, 2012

Dear Dr. Quinonez,

We hereby resubmit our manuscript, “Socioeconomic inequalities in cardiovascular mortality and the role of childhood socioeconomic conditions and adulthood risk factors: a prospective cohort study with 17-years of follow up”, for consideration for publication in the BMC Public Health.

We are happy with the positive evaluation of our manuscript by the Reviewers. We want to thank them for their good suggestions for further improvement of the manuscript. On the next pages, please find our point-by-point responses to the Reviewers and a description of the changes made. In the manuscript-file, we highlighted all changes.

If anything is unclear, don’t hesitate to contact me. We hope to hear from you soon.

Yours sincerely,

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Referee 1

This is a well-written manuscript examining socioeconomic determinants of CVD mortality in the Netherlands. The statistical analyses appear to be soundly conducted.

Thank you for your positive evaluation of our manuscript.

My main concern (major compulsory revision) would be that socioeconomic status in adulthood is defined solely upon respondents' highest attained educational level- presumably due to lack of a marker of respondent's own occupational status(?) . I feel that educational attainment is so closely associated with both childhood and adulthood SEP, that it is not possible to use education alone as a marker of adult SEP and that what you are explaining (or not) is the role of educational status rather than adult SEP as a determinant of CVD mortality. I'm sure that this is arguable! I realise that you allude briefly to this in your discussion, but to me it requires further unpacking.

We agree with the Reviewer that it is arguable which indicator is “best” for measuring socioeconomic position, as all common indicators (education, occupation, income, or an area-based measure) capture different aspects of SEP, and have its advantages and disadvantages. In the Netherlands, educational level has been evaluated as a good indicator for adulthood SEP, with the advantage (over occupational status and income) that it is available for both men and women. We also think that it truly measures something else then childhood SEP, which is in our study determined by the occupational level of the respondent’s father when the respondent was 12 years of age. We calculated the correlation between the two which is only .345 in our study, both among men and women. We extended the discussion on this topic on page 15.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Referee 2

Minor revisions

1) It's unclear as to why participants were excluded if they had heart disease within the preceding 5 years only. Given the chronic nature of CVD, it would be preferable to exclude all those who reported ANY history not just of heart disease, but of stroke. If this is not possible, a brief explanation should be provided

In the baseline questionnaire of 1991, respondents were asked, given a list of 24 diseases, which disease(s) they had experienced over the last 5 years. Among these diseases were severe heart problems, a heart attack and stroke. Based on this question, we excluded participants from the analyses with a recent history of heart diseases or stroke, but we do not know of any earlier history of heart disease or stroke. This is a small limitation of the study, and we now mention this in the Discussion: “In the baseline questionnaire, participants were asked whether they experienced severe heart problems, a heart attack or stroke over the last five years. We excluded participants from the
analysis who indicated they did, however, we do not know of earlier histories of CVD, and therefore, the analyses may still include participants with a history of CVD, which could have underestimated the contribution of behavioural factors (since CVD patients may have changed to a healthier lifestyle, while still having a higher chance to die from CVD).” (page 15)

2) Some more discussion/explanation is needed on:
   a) possible explanations for gender-related differences (i.e. material factors in men vs behavioural factors in women, plus the relative importance of physical activity and alcohol consumption in women)
   b) why material and behavioural factors explain more than psychosocial factors
   c) why childhood SEP not as ‘important’ as adulthood SEP

We agree with the Reviewer that these intriguing findings deserve some further discussion/explanation. Parts of the reasoning that you may find below are also included in the Discussion of the revised manuscript.

a) Behavioural factors were more important for explaining educational inequalities in CVD-mortality among women than among men. We are not aware of a biological mechanism that could explain why behavioural factors could be more strongly related to CVD mortality among women. However, the prevalence of several risk categories was also higher among women than men with lower adulthood SEP (e.g. for drinking no alcohol, physical inactivity and obesity), which may partly explain the higher relative importance for explaining inequalities in CVD mortality. The few other studies that reported on the relative importance of behavioural risk factors for CVD mortality for men and women separately[5, 9] found similar results with regard to smoking, in that smoking was relatively more important for men than women. Differences between men and women regarding the importance of other health-behaviours were less consistent. Strand and colleagues (2004) also showed that BMI contributed more to the inequalities among women, but they did not observe a gender difference in relative importance of physical activity (alcohol was not measured). 1

b) Psychosocial factors explained less of the inequalities, because, of the psychosocial factors that were investigated, only marital status and the use of sleep or anxiety drugs (among men) were associated with CVD mortality. Other studies also found psychosocial factors of less importance for inequalities in mortality than behavioural and material factors.2,3 Other psychosocial factors then the ones investigated in this study could be more important, and should be further investigated, e.g. locus of control, number of good friends, social participation, and social networks.

c) Childhood SEP is rather distal to CVD mortality, and there is a lot to happen between your father’s social position in your childhood (and related circumstances) and whether or not you die from CVD. We do see that childhood socioeconomic influences explain some of the inequalities in CVD mortality by adulthood SEP, namely via their influence on adulthood risk factors. One’s educational level, on the other hand, appears to be a good indicator for one’s adulthood SEP, and how likely it is that someone develops certain risk factors for CVD mortality, and with that, whether or not you will die from CVD. Therefore, adulthood SEP seems to be more strongly associated with CVD mortality than childhood SEP.

3) Marital/civil status - use only one term throughout
We now use marital status throughout the manuscript.

4) Define 'adulthood' (i.e. age)

We clarified this in the manuscript by including the following sentence: “In this study, all ‘adulthood’ measures (i.e. adulthood socioeconomic position as well as risk factors) refer to the age of 40 years or older (since the analyses were restricted to respondents in this age range at baseline), and ‘childhood’ refers to the age of 12 years.” (page 7)

5) Figure 1 needs a heading and more explanation

Figure 1 has an explanatory heading (page 25).

6) Page 13, paragraph 1, last sentence, beginning "However, educational...." is unclear. Could the sentence be rewritten so its meaning is clearer.

We removed the word ‘however’, and rewrote the sentence. We hope that the point we try to make is more clear now (namely, that the influence of childhood socioeconomic position may be underestimated when we correct for educational level as indicator for adulthood SEP, instead of another SEP indicator which may be less close to childhood SEP).

Level of interest: An article of importance in its field
Quality of written English: Needs some language corrections before being published
Statistical review: No, the manuscript does not need to be seen by a statistician.

Referee 3

This is an important and interesting study and analysis. It is also a really concisely and clearly communicated paper given the extent of the analysis. One real strength of the study is the availability of good quality self-report data for both adulthood and for a specific and consistent point in time at age 14. It is a strength of the study that it has sufficient sample size to restrict the analysis to participants age 40 or older at baseline, whereas many general population mortality studies look at baseline recruitment from a very large range of ages (for reasons of sample size) making it difficult to interpret the stage of life represented by baseline data and creating, really, far too large a range of follow-up time periods which reflect different life stages. The literature review is concise and appropriate and the fact that they address (succinctly and fairly) the competing hypotheses of the critical period and pathway models. The analysis is correct, well (and concisely) documented and easy to follow. No major concerns about the interpretation of findings.

Thank you for your positive evaluation of our manuscript.

Minor compulsory revisions:

-Numbers of observations in the models should be repeated in table titles or footnotes.

We have included numbers of observations in the table titles or in the tables.
- The methods state that missing values were retained as separate categories (there could be debate over the approach of retaining missing values as separate categories, but this reviewer accepts the practice). However, neither these categories nor the numbers of missing observations by covariates or across covariates in multiple survival analysis models are presented in the results tables. If the degree of list-wise deleted observations is small, it may be wise to merely allow the observations to drop out of multivariable models as is sometimes advocated by Sander Greenland and some others. Furthermore, if the global impact of missing observations is small then complicated procedures such as multiple imputation should probably not be entertained even should this come up in review. However, clarification about the extent of missing data and how missing answers were handled is essential.

For childhood socioeconomic conditions, we reported the HR for CVD mortality of the category of missing values in the table, since the proportion of missing values was high, i.e. 13.8%. The number of missing values for adulthood risk factors was generally small, i.e. ranging from 0.1% for physical activity to 5.7% for alcohol consumption among men, and from 0.5% for physical activity to 7.8% for alcohol consumption among women (we included this information in Additional file 1). Therefore, we decided to retain the missing values for each covariate as separate category in the analyses (except for those respondents with missing values for educational level (adulthood SEP), who were excluded from the analyses), and we are glad that the Reviewer agrees with this practice. We included a footnote with this information to Table 1.

- Under methods for alcohol consumption, please clarify if ‘units’ and ‘drinks’ mean the same thing.

We clarified this point in the methods for alcohol consumption.

- Vegetable ‘use’ should be vegetable consumption.

We corrected this.

- With respect to the contributions of smoking, alcohol use and other factors on mortality, for direct comparisons with other studies, it would be useful to comment on the population studied in terms of how high the prevalence rates were for smoking, obesity, etc, relative to other populations used in similar studies cited, or relative to the general European population at the same time. Within this manuscript, the reader should know if this city-specific sample (and those who agreed to participate) was particularly clean-living with respect to rates of smoking, obesity and heavy drinking as the absolute prevalence of risk factors do affect the attributable mortality.

We obtained prevalence rates of smoking (among people of 12 years and older) and overweight/obesity (among those 20 years of age and older) in the general population in the Netherlands in 1990 from Statistics Netherlands (http://statline.cbs.nl) (for physical activity and alcohol consumption, no comparable measures were available). A comparison of these prevalence rates in the general Dutch population with the prevalence rates in our study sample (aged 40 years or older) in 1991, showed that these rates were of similar magnitude. In our sample, rates of current smokers were 41.7% (men) and 28.0% women, compared to 42.8% (men) and 31.5% (women) in the general population. Further, rates of overweight/obesity were 46.0% (men) and 38.9% (women) in our sample, compared to 39.6% (men) and 30.6% (women) in the general population. The rates of
overweight/obesity are somewhat higher in our sample, but this could be due to the relatively older age (40+ years) compared to the age of the sample of the general population (20+ years). This indicates that the city-specific sample of our study is not particularly clean-living with respect to rates of smoking and obesity.

It is difficult to compare the prevalence rates in our study with those in other international studies, since prevalence rates are often not mentioned for men and women separately⁴, not available for each specific health-behaviour⁵–⁷, or only available stratified by own occupational level (instead of educational level) and adjusted for other factors⁸.

Most comparable data were found in a paper by Strand and colleagues (2004)¹, which included prevalence rates of risk behaviours in Norway in 1970 for men and women aged 35–49 from two educational classes, include the following numbers on current smoking:
- men: low education 58%, high education 43%;
- women: low education 39%, high education 30%.

These numbers are somewhat higher than in our sample (see additional file 1; men: low education 49%, high education 36%; women: low education 30%, high education 21%). This could be due to the survey year, as in 1991, already more people had stopped smoking compared to 1970.

Some of this information is included in the revised manuscript as well, see page

- The authors may be asked to weigh in more strongly as to whether they feel it is then more or less fruitless to seek to achieve CVD prevention by focusing on school-age children. There is theoretical merit in primary prevention of the behavioural risk factors in adulthood through intervention with youth and young adults, but hard evidence of impact on actual long-term disease prevention isn’t always available. However, there is increasing evidence shows that prevention less far upstream (within 10 years of what would be the onset of CVD and other diagnoses which share risk factors) may provide more bang for the buck.

We shortly addressed this point on page 16 of the Discussion.

Discretionary revision, but I’m strongly recommending this change as it would also add a new outcome and increase the impact of the paper:

- This reviewer advocates for a definition of normal weight with a lower limit in the order of 20, as opposed to 18.5. Increasingly, large cohort studies are appearing which have been able to subdivide the BMI 18.5-25 range into smaller groups with an additional (still arbitrary) cut-off of 20 becoming popular. Where this is done, it is common to find that mortality starts to increase below 20 in most middle-aged populations, relative to 20-25. (The point of increase may be as high as <22 in older adults, especially women, although nobody yet has the perfect cut-off across all populations and baseline ages). The lower limit of 18.5 really represents acute malnutrition and eating disorders. Any ‘normal’ weight definition that goes all the way from 18.5 to <25 is a mix of lowest risk for BMI and increased risk, and so makes for a poor reference category. The use of the 18.5 to <25 ‘normal’ range remains common, but the sample size here should allow for finer definitions, and this may result in greater explanatory power for adult BMI.
We want to thank the Reviewer for this interesting suggestion. We adjusted the BMI range accordingly, and now the new categories are: underweight (BMI<20), normal weight (BMI 20-25), overweight (BMI25-30), obese (≥30). The new results show that associations between BMI and CVD mortality are now stronger. Among men, BMI and CVD mortality are still not significantly related (adjusted for age, childhood socioeconomic conditions and adulthood SEP), although being underweight seems to have a protective effect for CVD mortality. However, among women, underweight is now associated with an increased risk of dying, just like obesity, whereas overweight and normal weight are not (see Table 1 for HR’s and 95% CI). We mention these new results in our manuscript in the Abstract (page 3), in the Results (page 13), in Tables 1 and 3, and in Additional file 1 and 2.

Level of interest: An article of outstanding merit and interest in its field

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, and I have assessed the statistics in my report.

Literature