Author's response to reviews

Title: Contribution of main causes of death to social inequalities in mortality in the whole population of Scania, Sweden

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Author's response to reviews: see over
Dear Sir/Madame:

Thank you for the comments from the referees. We greatly appreciate their insightful comments and constructive criticism. We have now incorporated the suggestions of changes by the reviewers in our manuscript with the name “Contribution of main causes of death to social inequalities in mortality in the whole population of Scania, Sweden” (MS: 1993632551890351). With the revised version is included a description of the changes made where we respond point by point to the comments of the reviewers.

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Sincerely,

Maria Rosvall
Description and Motivation of the changes made to our manuscript with the name “Contribution of main causes of death to social inequalities in mortality in the whole population of Scania, Sweden” (MS: 1993632551890351) after consideration of the suggestions of changes proposed by the reviewers. Additional text in the manuscript has been underlined:

Reviewer #1:

Major compulsory revisions:

1. The former sentence in the abstract: “As expected, diseases with well established mechanistic links with SEP made major contributions to the mortality differences seen.” Has been changed into: “In agreement with the distribution of main causes of death, CHD, with well established mechanistic links with SEP (smoking, dyslipidemia, hypertension), made major contributions to differences in overall mortality.”

2. The sentence in the Introduction section on line 2-3 “First, it is important to recognize that associations between social inequality and health inequality are contingent on mechanistic links between social position and the major risk factors for different causes of death…” has been changed into: “First, it is important to recognize that social inequalities in health are contingent on mechanistic links between social position and the major risk factors for different causes of death…”

3. The sentence mentioned above has been extended to also include the following phrase: “...causes of death and on the social distribution of such risk factors.”

4. The former sentence in the Introduction section line 6-8: “It follows that, secondly, to most efficiently reduce social inequalities in mortality, it is important to establish which causes of death contribute most to socioeconomic mortality differentials”. has been changed into “It follows that, secondly, to more efficiently reduce social inequalities in mortality, it is
important to establish which causes of death contribute most to socioeconomic mortality differentials”.

5. A short summary of the results of earlier studies is now provided in the Introduction section on p. 4:” In summary, these studies generally show higher mortality rates among those in lower SEP compared to those in higher SEP, with regard to causes of death such as CVD, cancer, diabetes, chronic obstructive pulmonary disease (COPD) and external causes.”

6. We are sorry if the terminology was not clear. We are not criticising earlier studies for failing to focus on various diseases, as this is what causes most deaths in the World (much fewer deaths are due to external causes such as for example accidents or suicide). What we wanted to say with the sentence mentioned was that earlier studies have investigated the association between SEP and mortality, however, only two studies have investigated the proportional importance of various disease entities on socioeconomic inequalities in mortality in specific age groups and no earlier study have been made on this issue using the whole population as in our study. “Main causes of death” denotes the diseases or external causes that causes the main part of all deaths in a population. We have now rewritten the sentence on former line 8 (now line 9) talking about main causes of death to clarify what we intend to say: “Earlier studies have investigated patterns of the main causes of death, i.e., diseases or external causes, to socioeconomic inequalities in mortality (4-14). In summary, these studies generally show higher mortality rates among those in lower SEP compared to those in higher SEP, with regard to causes of death such as CVD, cancer, diabetes, chronic obstructive pulmonary disease (COPD) and external causes. However, few studies have specifically investigated which diseases contribute the most to existing socioeconomic mortality differences in specific age-groups (9,12) and none were in samples of the whole population, where selection bias is minimized.“
7. We appreciate the reviewers comment on the fact that the measure of occupation and relation to the workforce is measured only once in time and the fact that there might be changes in occupational status and relation to the workforce over time. However, unfortunately, we are not able to use a longitudinal approach in this study, due to the fact that we can only get these data on some of the age groups included in our study. We have therefore added a comment on this in the Discussion section on p. 18: “The cross-sectional measurement of occupational status and relation to the workforce at one point in time gives room for potential misclassification. People may for example change occupations or move into the workforce after having completed high school- or university studies. However, potential misclassification of SEP would be expected to be nondifferential and would thus lead to an underestimation of an effect on mortality.”

8. Each deceased person in Sweden gets one underlying cause of death on the death certificate. The underlying cause of death is defined as a. the disease or injury that initiated the chain of diseases that finally resulted in death or b. the circumstances involving the accident or the act of violence that caused the lethal injury. In epidemiological studies the different causes of death are often grouped together into rather large categories “major causes of death” with different kinds of similarities such as cardiovascular diseases, cancer diseases, where the categorization often is done according to national or international recommendations, to get enough power to be able to perform analyses. If using a bigger datamaterial including lots of cases it is also possible to break these causes of death into smaller subgroups within these larger entities, i.e., specific causes of death as for example breast cancer, lung cancer, stroke...This is now clarified in the text in the Methods section on p. 7. “Each deceased person in Sweden gets one underlying cause of death on the death certificate. An underlying cause of death is defined as a. the disease or injury that initiated the chain of diseases that finally
resulted in death or b. the circumstances involving the accident or the act of violence that caused the lethal injury. These underlying causes of death were used in the categorization into major groups of causes of death and specific causes of death. The study population was followed with regard to all-cause mortality, major groups of causes of death (cardiovascular, cancer, external causes, psychiatric mortality and chronic obstructive pulmonary disease (COPD)) and specific causes of death within the major groups of death (i.e., coronary heart disease and stroke within CVD mortality, lung cancer, prostate cancer, breast cancer, and colorectal cancer within cancer mortality, and suicides and traffic accidents within mortality due to external causes).”

9. The second sentence on line 2-3 in the Discussion section has been changed into: “With an exception for younger age groups (aged 40 years or less), CVD and cancer made the largest contributions to these mortality differences.”

10. We have now re-run the analyses for overall mortality including all three groups comparing those outside the workforce to those in non-manual occupations to look at the full social spectrum. The results from these analyses are now shown in figure 3 and 4 and also presented in the Result section on p.14: “We also conducted analyses comparing those outside the workforce to those having non-manual occupations with regard to overall mortality. As seen in figure 3, the relative mortality differences between those outside the workforce and those holding non-manual occupations were greater than the differences seen between those holding manual or non-manual occupations in all age groups in both men and women. A similar pattern was seen for the absolute differences in overall mortality as shown in figure 4.”

We have also rewritten part of the Discussion section on former p.16 (now p.17) which now says: “Being outside the workforce was associated with a strongly increased risk of future
mortality compared to being inside in all age groups in both men and women. When interpreting this increased risk one should consider that the former group was heterogeneous including for example housewives as well as disability pensioners and students. The latter which would be expected to have relatively low mortality rates. These mortality differences were generally greater than the differences seen between those holding manual or non-manual occupations. When comparing mortality rates between those outside the workforce and those holding non-manual occupations, the differences were even bigger. This was especially true when using absolute measures of effect, but also when using relative inequality measures. Thus, the inequalities in mortality seem to be greater according to workforce participation than according to occupational category.”

11. We appreciate the important comment from the reviewer regarding the accuracy of the causes of death on the death certificates. Swedish statistics on causes of deaths are among the oldest worldwide. They go back to 1749 when a nationwide report system was first introduced. The mortality register encompass 97 percent of all deaths in Sweden and the census participation rate varies between 97-99 percent. Thus, there is no reason to believe that incomplete retrieval of cases biased the results. The main source of statistical unreliability is the accuracy of the underlying cause of death that the physician writes on the death certificate. We now mention potential problems of accuracy of causes of death in the Discussion section on former p. 18 (now p.19): “The quality of the data on causes of death also depends on the accuracy of the underlying cause of death that the physician writes on the death certificate. It is widely known that the data on causes of death generally are more accurate in younger than in older people depending on the fact that older people often have multiple diseases where it can be harder to determine the underlying cause of death than in younger subjects together with the fact that younger subjects are more frequently being autopsed after death than older
people (32). Such a misclassification might theoretically have an effect on the absolute levels for different causes of death, and where the use of more narrow classification categories such as specific causes of death would be more prone to misclassification than the use of broader categories such as major causes of death. However, there is no obvious reason to believe that this kind of potential misclassification would differ by SEP in a country like Sweden with a well-developed social security system.”

12. We have now included potential reasons why CVD made the largest contribution to socioeconomic inequalities in mortality on p.16-17 in the Discussion section: “This might partly be attributed to the fact that cardiovascular diseases constitute about half of all deaths in Sweden, with CHD being the largest disease entity within the category of cardiovascular diseases. Furthermore, CHD has well established mechanistic links with SEP, through smoking, dyslipidemia, and hypertension.”

We have also added to the Discussion section on p. 15 potential reasons why the relative contributions of different causes to the socioeconomic inequalities in mortality vary over the lifecourse: “The contribution of specific causes of death to excess mortality by SEP changed substantially with age, with CVD becoming more important in older ages, whereas the opposite pattern was seen for psychiatric disorders and external causes. This is probably mostly attributed the differing distributions of main causes of death at different ages.”

Regarding potential intervention strategies suggested by the results we have added two sentences to the Discussion section to more specifically address this issue on p.16: “The results regarding the proportional role of specific causes of death for understanding SEP inequalities in overall mortality in various age groups and sex specific groups is of importance
since it might broaden ideas about potential preventive strategies to reduce social inequalities in health. The results from our study show that different causes of death with widely different mechanistic links with SEP are of importance to social inequalities in health in different age groups. Thus, the focus of preventive programs to reduce social inequalities in health should vary by age.” Furthermore, the last sentence in the same paragraph on p.16 also discuss the importance of further knowledge of the association between SEP and also less common diseases/external causes to be able to more successfully intervene on social inequalities in health. “Thus, an increased understanding of the mechanisms connecting SEP with diseases that are less common than CHD might also be important to be able to more successfully intervene on socioeconomic health differences.”

Since there only two of the mentioned studies that have specifically investigated which diseases contribute the most to existing socioeconomic mortality differences in specific age-groups (which is also mentioned in the introduction section on p.4) , it is hard to do comparisons with the results from all the mentioned studies with the results from our study. Therefore, we have chosen to compare our results with the results from the two studies that performed similar analyses. One of these studies is the study by Kunst et al. mentioned in the text in the Discussion section on p. 15: “. The relative inequalities found in our study correspond well to those found in the study by Kunst et al. investigating socioeconomic mortality differences in men aged 45-59 years (9). In the study by Kunst et al. the relative inequalities between Swedish non-manual and manual workers with regard to overall mortality, CVD, cancer and external causes were 1.41, 1.36, 1.18 and 1.76, respectively. Corresponding relative inequalities among men aged 51-60 years in our study were 1.4, 1.4, 1.3 and 1.7, respectively. “ and on p.18: “The classification is in agreement with the Erikson, Goldthorpe and portocarero (EGP) scheme used in the study by Kunst et al. (9) based on work
tasks, job responsibility levels and employment relations, but also on the educational background needed (15). “The other study is the one by Huisman et al. mentioned in the text on p. 16.” However, as shown in the international study by Huisman et al. (14), stroke and other types of cardiovascular diseases also made substantial contributions to the mortality differences.”

Minor points:
13. The sentence in the abstract on line 17 “…differences seen between manuals and non-manuals”. has been changed into:”…differences seen between those holding manual and non-manual occupations”. A similar change was made on p. 11, 15 and on p.20 in the conclusions.
14. The sentence on former p.11 (now p.12), results section: ”Those outside the workforce showed markedly higher relative inequalities compared to…”. has been changed into: “”Those outside the workforce showed markedly higher mortality rates compared to…”
15. The sentence in the Discussion section on p.15: “The smaller contribution of cancer in older ages has been argued to be referred to the relatively smaller contribution of lungcancer due to the socioeconomic reversed pattern of smoking seen from the 1940s through the 1960s in the Western world (14,20).” has been rewritten and clarified and now says: “The diminished contribution of cancer in older ages has been argued to partly be referred lungcancer and breastcancer. Subjects in older age groups with higher SEP have lungcancer to a similar extent as subjects with lower SEP due to the socioeconomic reversed pattern of smoking seen from the 1940s through the 1960s in the Western world (14,20). Furthermore, there are studies that have shown that the most common type of cancer seen in women, namely breast cancer, is more common in higher SEP groups (13,14,21), even though some studies have shown that socioeconomic differences in breast cancer mortality are currently changing and the previously observed positive gradient has disappeared”.
16. The sentence on former p.16 (now p.17-18) :” Thus, the social inequalities by workforce participation seem to be associated with a greater health problem than the social inequalities seen among those inside the workforce.” has been rewritten and now says: “Thus, the inequalities in mortality seem to be greater according to workforce participation than according to occupational category.”

17. The sentence on former p.16 (now p.18): ” Even though there was a pronounced role for CVD, contributing to the mortality differences, the role of other specific causes besides cardiovascular, cancer, external causes or psychiatric diseases were relatively greater” has been clarified by adding: “according to workforce participation than according to occupational category.” At the end of the sentence which now says:” Even though there was a pronounced role for CVD, contributing to the mortality differences, the role of other specific causes besides cardiovascular, cancer, external causes or psychiatric diseases were relatively greater according to workforce participation than according to occupational category.”

18. The sentence in the Discussion section, former p.17 (now p.18) has been rewritten and clarified and now says: “Furthermore, with an exception for younger ages, breast cancer showed higher mortality rates among women outside the workforce than in women inside the workforce.”

19. The sentence in the Discussion section on former p.18 (now p.19):” Misclassification of end-point is a potential cause of bias.” has been rewritten and now says: “Another methodological issue that needs to be addressed is the classification of end-point.”

Discretionary Revisions:

In figure 1, we wanted to show the relative contributions of different causes of death in different age groups in the population investigated, i.e., those holding manual or non-manual occupations so that the reader could have this as a reference when interpreting the relative
contributions of different causes of death to the socioeconomic mortality differences. We also made a figure for the whole population, but as the distribution of relative causes of death was similar to that seen for those holding manual or non-manual occupations, we chose not to show this in the text. However, following the comment of the reviewer we have now chosen to have it in the text as Figure 2.

Even though gender differences is not the scope of this article, we think it would be interesting just to show these differences in overall mortality. We do not further discuss these differences in the Discussion section.

Reviewer #2:

Major comments:
The calendar years of the study, 1991 to 2002, has now been given in the abstract and at the beginning of the paper.

“The social situation of those aged 20 years or less was measured according to household occupational status.” This sentence has been added to the introduction section, last paragraph and is also included in all tables.

We have now added a comment about the fact that there in the age group 21-30 years probably are included many students who would be expected to have relatively low mortality rates. on p. 17: “When interpreting this increased risk one should consider that the former group was heterogeneous including for example housewives as well as disability pensioners and students. The latter which would be expected to have relatively low mortality rates.”
The notion of breast cancer being more common in higher SEP groups during recent years is more thoroughly discussed in the Discussion section on p.16: “Furthermore, earlier studies have shown that the most common type of cancer seen in women, namely breast cancer, is more common in higher SEP groups (13,14,21), even though some studies have shown that socioeconomic differences in breast cancer mortality are currently changing and the previously observed positive gradient has disappeared (22).”

**Minor comments:**

Abstract, to was missing …”to” has been added.

Chronic obstructive pulmonary disease has been added on p.7 before the acronym COPD.

Study population on p.5 “(about one million every year” has been changed into: “(about one million).”

The word artifact has been taken out and replaced with result and the sentence now says: “The declining relative inequality with age is partly a result of the increasing absolute death rates in both socioeconomic groups.”

**Discretionary Revisions:**

We thank for the reviewers comment on the suggestion of having more detailed information on causes of death in tables 2 and 5. However, we choose to keep the tables as they are - not to make the table section too complex to read.