Author's response to reviews

Title: Socioeconomic differences in cancer survival: The Norwegian Women and Cancer Study

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Author's response to reviews: see over
Regarding the manuscript MS: 2585491602339896  Socioeconomic differences in cancer survival: The Norwegian Women and Cancer Study

Thank you for your mail of 26 January 2009 and the referees’ comments, which we believe have contributed to an improvement of our manuscript.

We hereby resubmit our paper. The paper has been revised, and we have endeavoured to edit the text carefully following the referees suggestions, which are highlighted in red below, with underlining and italics font. The referees’ comments are cited with Arial font.

Due to minor corrections of the follow-up data, some estimates have altered slightly from the first version of the manuscript.

Our response can be summed as follows:

**Referee 1**

Table 1 presents only percentages: I would prefer to have the values too. Further T1 is actually 2 tables (this may be an error of the PDF) - should they be Tables 1a and 1b?

Table 1 is now splitted into table 1a and table 1b, and the total number of women in each category is displayed.

In the discussion, the advantage of this study being prospective is not adequately made: I'd use that precise word in the second paragraph.
The second paragraph has been changed, precising that the study is prospective, according to the referees’ comment. It reads now as follows:

*As The NOWAC Study is prospective, the information on lifestyle and behaviour was collected before cancer diagnosis, and therefore, is not subject to recall bias, which is advantageous according to the understanding of causality.*

One limitation not mentioned is the fact that it is a women-only study - does that make the income analysis any less solid?

We do not believe so: women have been far less studied than men in relation to socioeconomic status (SES) and cancer survival, and our study provides important information to fulfill this information gap.

The following sentence is added to the discussion section, page 10, line 3, which further clarifies why education may be a preferable measure of SES:

*Education is probably the most adequate measure of SES, particularly among women; it applies to every adult individual, and is more stable over one’s lifetime than income [18].*

In the discussion, I would have preferred more on why this study suggests that smoking and stage accounts for the SES survival differences. If it’s stage, then surely there must be diagnostic issues here (even if references 7&8 think not).

We have made some changes in the text to clarify the key message of our study; namely that smoking appears to be an important predictor of SES differences in cancer survival, whereas stage distribution does not.

*The results of our study question the distribution of tumour stage at diagnosis as a consistent mediator of SES variation in survival, but rather emphasize the influence of lifestyle factors such as smoking. Indeed, in our study, smoking status explained about 51 % of mortality risk difference between the upper and lower educational groups after adjusting for age, stage, and co-morbidity prior to diagnosis.*

Furthermore, the smoking explanation is not just that smoking causes more and nastier cancers, it also causes co-morbidities. I remember some years ago a chest physician saying half his lung cancers died of myocardial infarctions (I suspect he overstated the percentage!)
In order to clarify that only deaths caused by cancer are considered in the analyses of survival, the following is added to the last paragraph of the introduction, page 3, line 19:

*We studied both overall survival, and survival for selected sites, using information from death certificates to identify the cancer deaths.*

As co-morbidity is a relevant issue in this study, we have included prevalence of certain diseases at enrolment as a covariate in the analysis of survival by education.

The following is added to the methods section, page 6, line 19:

*Co-morbidity prior to diagnosis (prevalence of cardiovascular or coronary heart diseases, or poor perceived health) is included in the analysis of survival of all solid tumours by years of education.*

The following statement is added to the discussion section, page 10, line 12:

*Despite our ability to adjust for prevalence of certain diseases or poor perceived health at study enrolment, we cannot completely rule out the potential influence of co-morbidity on cancer survival.*

**Referee 2**

As there have been a number of previous studies on this subject and it is now accepted that survival from cancer is significantly affected by SES, the authors of this study need to indicate why this study is needed and what is original about it.

I think the discussion is far too long compared to the results section. They should have reported more of the results in the text to compare to other studies rather than just make general statements about the results.

We complied with the referees’ suggestion by both removing old text and adding new text to the discussion section of this revised article. The following paragraph was removed from the discussion, page 9:

*However, for both education and income all estimates of relative risks and linear trends in risks levelled off after further adjusting for tumour stage and smoking status before diagnosis, with the exception for colorectal cancer. The educational differences in survival of this site*
were weakly associated with consumption of alcohol. Similar differences in survival of colorectal cancer did not emerge in the analysis by income probably because the unfavourable effect of alcohol among the highest income groups was counterbalanced by a favourable distribution of stage.

We added in the discussion section, page 10, line 16, a reference to the following recent Danish study:

_The increased mortality risk in cancer patients of low SES groups observed in our study confirms findings by several previous studies [2-9]_

At page 9, line 24, one reference has been added:

_Different SES measures are dissimilarly related to underlying causal factors and cannot be used interchangeably [10,11]._

At page 10, line 19 the following statement with references is inserted:

_Our finding of an improved survival by high SES for ovarian cancer does neither seem to be consistently evidenced [7,12,13]._

At page 11, line 5 is extended with one additional reference:

_Neither differences in timing of diagnosis nor differences in tumour aggressiveness have been evidenced to explain the variation [12,13], but a recent Danish study reports that patient characteristics predict delay in cancer diagnosis, among others in female smokers [14]._

There should be some improvement in the presentation of the results. The authors indicate that they have carried out Cox regression analysis with hazard ratios but report relative risks in the tables and results.

Indeed, this is what we did, which is technically correct. For clarity we added the words “the reported” is added to line 4, page 6:

_The hazard ratios are interpreted as estimates of the reported relative mortality risks (RR)_

In the results section the authors initially report p values, although say p=0.04 is non-significant (last sentence on page 7) and then on page 8 report chi-square results and spearman correlation coefficient.
P values are now added to the chi-square results and the Spearman correlation coefficient reported in the last paragraph of the results section, page 8.

The background section states that most studies previously carried out on this topic were ecological studies, but they are not. They include cohort studies too.

In the background section, page 3, line 3, the words “The majority” is replaced with “A number”. The word “cohort” is added to the second sentence. We have also added a statement concerning the limited number of previous studies with information on lifestyle. The paragraph reads now as follows:

*A number of these are ecologic studies using geographical area based measures as SES indicators (comparing richer with poorer areas). Others are hospital-based or record linkage cohort studies with individual information on socioeconomic status measured by socioeconomic group, income or level of education. Occasionally, health insurance status has been applied as a proxy of SES [5,6]. One cohort study among men has been able to consider lifestyle factors such as smoking and alcohol consumption according to SES and cancer survival.*

There is now no doubt that SES affects survival, so I am not sure about the point of this study. Perhaps the authors could highlight the new and original results from this study that are different to previous studies or at least compare results to other similar studies. There is a lot of text for the methods and discussion section but only a very short section for the actual results.

The last paragraph of the background section, page 3, has been changed in order to emphasize the major advantage of our study:

*We present here results from a prospective cohort study where we evaluated how socioeconomic conditions at time of recruitment affect the likelihood of cancer survival. We studied both overall survival, and survival for selected sites. The comprehensive information*
collected in The NOWAC Study enables us to assess individual’s lifestyle before diagnosis besides tumour characteristics as potential confounding factors of socioeconomic variations in cancer survival.

We have given more specific results for the effect of adjusting for stage distribution, co-morbidity, and smoking status, respectively. The results section is expanded to report more relative risk estimates.

I think it would be useful to have more information about the questionnaire and how it was validated.

The last sentence has been added to the end of the paragraph about The NOWAC Study in the methods section, page 4

The questionnaires as well as other details of the cohort can be found at http://uit.no/kk/NOWAC/. The validity of The NOWAC Study has been assessed [15].