Author's response to reviews

Title: Socio-economic class, rurality and risk of cutaneous melanoma by site and gender in Sweden.

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Version: 2 Date: 8 October 2007

Author's response to reviews: see over
Dear editor

Thank you for allowing us to send a revised manuscript addressing the reviewers' comments. We also added in the text the information on competing interest, authors' contribution and acknowledgements, and a English-mother tongue professional translator has corrected again the manuscript, as one of the reviewers suggested. We have also complied with the BMC checklist format.

In this cover letter we include a point-by-point response to the reviewers’ comments and suggestions.
Reviewer’s report
Title: Socio-economic class, rurality and risk of cutaneous melanoma by site and gender in Sweden.
Version: 1 Date: 21 August 2007
Reviewer: Adele Green

General
The association between Socio-economic class and incidence of melanoma is of interest to public health in a practical way if it is able to shed light on causation mechanisms and/or prevention. The authors have therefore set out to explore two possible effect modifiers of the association, rurality of residence of people affected and anatomic site of the melanoma. These questions potentially could yield some useful information but the present paper had several limitations, the chief ones being that the methods were one step removed from the nominal aims of the study, and that their results and interpretation did not really add any truly new insights and were in fact rather circular.

Response:

Firstly, we should like to thank the reviewer for her time and attention. Yet, we must disagree with her opinion on this paper. Our stated aim was to ascertain whether risk distribution by socio-economic class or town size was different among men and women by anatomical site, in a major-sized, ten-year follow-up covering an historical Swedish cohort of over 1,000,000 working women and almost 1,900,000 men. One of our main results (and conclusions) is that this cohort displayed no differences in risk of head and neck melanoma by socio-economic sector or by town size in either sex. We are thus at somewhat of a loss to see how this could be considered a circular result.

Title: Socio-economic class was measured by a proxy, namely occupational sector in registered group data. While this may be satisfactory for hypothesis generation, it is a blunt tool for exploring finer points of the association being aimed at here, which normally required individual level data to be studied to get a true measure and thus understanding of the influence of Socio-economic class.

Response:

Although this paper should, in our opinion, be viewed from a “hypothesis-generating” stance, we used information on the occupation of each individual in the cohort, as described in our previous studies, in which we sought to identify occupations with increased incidence of melanoma among Swedish men and women. We have endeavoured to explain this more clearly in the text.

Occupation is among the indicators most commonly used to measure socio-economic status. It is regarded as a simple, pertinent and reliable indicator of the relative position of the individual in society, also linked to educational and income levels, which defines access to resources, as well as constraints that can have implications for health and mortality. In the Nordic Classification of Occupations, each occupation is represented by a three-digit number. The first digit of this classification allowed us to classify each individual into 10 major occupational sectors (0-9). The code represents occupations rather than industrial sectors, e.g., an engineer working in a steel factory is included in sector 0 - professional/technical workers— and not in sector VII or VIII, which together include all blue collar workers working in the same factory. Hence, this categorisation enables manual to be distinguished from non-manual occupations, which often require longer education and are associated with higher socio-economic status.

One of the main reasons for the study was to give new insights about the association in women, but occupational sector is a much poorer indicator of Socio-economic class status in women than men, especially 35 years ago when at baseline status was determined for this study.

Response:

This problem was discussed in the text. Although occupational sector might be a poorer indicator of socio-economic status in women than it is in men, in our opinion this does not preclude risk distribution in women being studied by the occupational sector to which they belong.

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1 Liberatos P, Link BG, Kelsey JL: The measurement of social class in epidemiology. Epidemiol Rev 1988, 10: 87-121
2 Galobardes B et al. Indicators of socioeconomic position (part 1). Journal of Epidemiology and Community Health 2006:60:7-12; doi:10.1136
The issue of measuring socio-economic class in women is still unresolved. Some authors, such as Goldthorpe, defend the view that women should be assigned their husbands' status, as they consider that women's personal working conditions are dependent on their role as housewives and their partners' social class. Others, in contrast, argue that this is the result of a patriarchal view of society, because a woman's own occupation partly defines her role –both within the household and in the labour world- and, in a relevant proportion of cases, her income; accordingly, this school proposes that women's own jobs be used. Finally, a third group of researchers prefer the household socio-economic estimator. In Sweden, the proportion of working females was already close to 50% in the 1970s.

5 Liberatos P, Link BG, Kelsey JL: The measurement of social class in epidemiology. Epidemiol Rev 1988, 10: 87-121
Our occupational sectors were defined using 1970 occupations. The above-mentioned trend mainly reduced socio-economic differences among the groups during our follow-up period, yet even with this increased homogenisation there was an association between melanoma and occupational sector.

Insofar as town size is concerned, Hakansson reported that in Sweden the propensity to migrate decreased slightly during our follow-up period: in all, from 1971 to 1996 the number of people migrating across municipal borders decreased from 5.1% to 4.5% of the population. Migration led to dispersion of the population in the 1970s. Thereafter, the larger urban areas had a net inward-migration in the first half of the 1980s but this was followed by a net outward-migration in the latter half of the decade.

Again, we would like to reiterate that changes in occupation or residence would not account for the specific pattern found in head and neck.

The study period and study population: The study period was 1970 to 1989. How relevant are the findings today, 20 to 30 years later? Also the homogeneity of the Swedish employed population may have been a very large disadvantage in that the range of sex-specific outdoor behaviours would not be generalisable to many populations around the world. It would be helpful for the authors to discuss the relevance and generalisability of the data presented to melanoma in the Western world at present.

Response:
As socio-economic associations have to be tested on real populations, it is always difficult to extrapolate results from one society to another. Sweden may represent an unusually successful mix of very high standards of living, minimal income inequality, and low unemployment, with high rates of female occupation, yet it probably has many things in common with other North European countries. Accordingly, if such differences in occupation-related risk can be found in a country like Sweden, this association might well be stronger in other populations with greater social differences, such as the German or British populations, who have also been in the habit of spend holidays abroad since the 1970's. Nowadays, low-cost airlines and all-inclusive package holidays have made trips to sunny destinations affordable for many people. Sunbed use has also become more common. This increasingly generalised UV exposure may perhaps lead to a more uniform distribution of risk by social class or town size in the future. Moreover, the association with social class may even be reversed, should sun-protective behaviour become the norm among higher social strata, much in the same way as has happened with tobacco use.

However, we would like to point out that, if travel to sunny destinations can in part explain this socio-economic gap in risk, the lack of association for head and neck would seem to suggest that melanoma at this anatomical site does not have any relationship with this, thus pointing to a different pattern of exposure which might trigger the neoplasm at this location.

Results:
Many of the occupational sector (“Socio-economic class”) gradients described were not gradients but rather dichotomous level of association with melanoma ie 0-III (professionals and sales workers showing similar levels of risk) vs IV-IX. The authors need to discuss this and show trend tests if they are claiming gradients exist in table 1 data.

Response:
The reviewer is right when she states that occupational sectors do not follow a statistically significant trend. Although occupational sector categories reflect socio-economic differences, this is not a quantitative way of measuring socio-economic level. Hence, occupational sector was introduced into the models as a categorical variable (with dummy variables), to obtain a risk estimator independently for each sector. Each sector was compared to the average incidence for the cohort, in each sex. The results showed that in men the highest risk was in sector I –administrative and managerial work- the lowest was in production, transport and agriculture, whilst the service sector (IX) ranked in an intermediate position. These differences were not as evident in women.
Reviewer’s report
Title: Socio-economic class, rurality and risk of cutaneous melanoma by site and gender in Sweden.
Version: 1 Date: 28 July 2007
Reviewer: Erika Richtig
Reviewer’s report:
General
In this manuscript Pérez-Gómez et al. analyse the relative risk of melanoma in Swedish male and female workers with special regards to socio-economic status, town size, gender and site.

MAJOR COMPULSORY REVISIONS (THAT THE AUTHOR MUST RESPOND TO BEFORE A DECISION ON PUBLICATION CAN BE REACHED)

1) There have been several publications concerning the clustering of melanoma in higher socio-economic groups in Sweden, which are not mentioned in the reference list (e.g. Hemminki et al.: Level of education and the risk of cancer in Sweden, Cancer Epidemiol 2003; Hemminki et al.: socio-economic factors in cancer in Sweden, Int J Cancer 2003). Those publications use the Swedish Family Cancer Database including the Swedish Cancer Registry, as this manuscript does also. The authors should state the difference in their findings with regard to those publications in the discussion.

Response:
As suggested, we have added these references and a comment on their results. They were also included in the comprehensive review on socio-economic factors included in the reference list. Hemminki et al. study the association between education or socio-economic class and the main types of cancer (lung, breast, prostate, as well as melanoma) but do not specifically discuss melanoma. The main difference between our paper and those cited is that the latter do not study the association between melanoma and socio-economic class for each anatomical site of melanoma.

2) The same authors have already published the occupational risks by anatomic site of men and women in Sweden. What is new in this manuscript?

Response:
In our previous studies, our aim was to identify which occupations –dentists, furriers, etc.- registered the highest risks of melanoma in men and women, with socio-economic status and rurality just being considered as possible confounding factors. In this paper, however, the main objective was precisely to study the relationship between melanoma and these two variables.

3) The method is not described clearly enough:
   a. the authors should explain, if they have taken all melanomas (also melanomas in situ?) or only invasive melanomas.

Response:
Melanoma in situ is also included. This information has now been added to the text.

   b. For me it is not clear when the melanomas in the Swedish working population were diagnosed: after the census 1970? or between 1960 and 1970 and followed up after 1971? Because, if melanomas occurred later, occupation and residence might have been changed since the census 1970. Was the occupation and residence re-evaluated at time of melanoma diagnosis?

Response:
This is a retrospective cohort. The follow-up of all melanoma-free members of the Swedish working population began in 1971. We have explained this in detail in the answer to the first reviewer. Occupation and residence were not re-evaluated at the date of diagnosis. Nevertheless,

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the latency period required to develop the neoplasm renders this latter evaluation of little consequence with regard to the association tested.

4) The geographical areas (Northern Sweden, Central Sweden and Southern Sweden) were mentioned in the methods, but in the results the geographical areas and their influence as environmental regular sun exposure markers are missing. Was there an influence on melanoma sites? Especially for the lower limb in women and head/neck melanomas, as the lack of influence of socio-economic class and town size on head/neck melanomas is one of the most clear results of the study.

**Response:**

As we explain in the Material and Methods section, the multivariate model included geographical distribution as an additional confounder. This Table shows the estimated risks of melanoma for both sexes by geographical area and anatomical site.

<table>
<thead>
<tr>
<th></th>
<th>All cases</th>
<th>Head and neck</th>
<th>Thorax</th>
<th>Upper limbs</th>
<th>Lower limbs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Py.</td>
<td>C</td>
<td>RR</td>
<td>95% CI</td>
<td>C</td>
</tr>
<tr>
<td><strong>Men</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Northern Sweden</td>
<td>7937136</td>
<td>930</td>
<td>0.68</td>
<td>0.63 - 0.74</td>
<td>130</td>
</tr>
<tr>
<td>Central Sweden*</td>
<td>12016038</td>
<td>2304</td>
<td>1.00</td>
<td>269</td>
<td>1.00</td>
</tr>
<tr>
<td>Southern Sweden</td>
<td>13405994</td>
<td>2953</td>
<td>1.24</td>
<td>1.17 - 1.31</td>
<td>328</td>
</tr>
<tr>
<td><strong>Women</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Northern Sweden</td>
<td>4429700</td>
<td>485</td>
<td>0.67</td>
<td>0.60 - 0.75</td>
<td>59</td>
</tr>
<tr>
<td>Central Sweden*</td>
<td>8081657</td>
<td>1357</td>
<td>1.00</td>
<td>161</td>
<td>1.00</td>
</tr>
<tr>
<td>Southern Sweden</td>
<td>6297394</td>
<td>1756</td>
<td>1.30</td>
<td>1.21 - 1.40</td>
<td>179</td>
</tr>
</tbody>
</table>

Py: person-year CI: Confidence interval  
Blue text denotes RR<1 and p<0.05  
Shaded sectors denote RR>1 and p<0.05  

* Reference category

As this Table shows, North Sweden invariably registered a statistically significant lower risk of melanoma than did Central Sweden. In addition, there was a significant excess risk in the south, more uniform across the different sites in men and, with the exception of head and neck, in women. We did not add these risk estimates in the paper as we think they might distract the reader from the main results.

5) Authors should give some data on the melanomas, available by the Swedish Cancer Registry like shown in other publications (e.g. Lindholm et al.: invasive cutaneous malignant melanoma in Sweden 1990-1999, Cancer 2004): tumor thickness, ulceration with regard to location, gender and town size.

**Response:**

Although the Cancer Registry probably has these data, the database used for this analysis—the result of combining the 1960 and 1979 censuses and the cancer registry—does not include them, and so we are unable to add this information.

6) In the discussion section, last paragraph, authors should state a possible bias when taking only workers in their analysis and not state "to study melanoma incidence patterns by socio-economic risk and rurality..."

**Response:**

This has been commented upon in a previous paragraph on this. The mistake indicated by the reviewer has been corrected.
MINOR ESSENTIAL REVISIONS (SUCH AS MISSING LABELS ON FIGURES, OR THE WRONG USE OF A TERM, WHICH THE AUTHOR CAN BE TRUSTED TO CORRECT)

1) Table 1 should be changed in "all cases" as cutaneous melanomas with multiple sites (several melanomas in the same patients?)- YES- and non-specified locations should be abandoned.

Response:
We sought to study melanoma as a whole as well as by site. When we state “all cases” in Table 1, we are really including all cases of melanoma. Multiple sites in an individual subject or cases with unspecified location are also melanomas and, as such, are considered in the analysis. These cases were only excluded in the site analyses.

2) There should be a Table 2 with specific melanoma data (tumor thickness with regard to site, gender and occupation).

Response:
As already explained, our database does not include this information and we are therefore unable to add the proposed table to the paper.

3) Reference list should be shortened and Swedish publications (see major revisions) should be included.

Response:
We have added the references suggested. The reference list has not been shortened since another reviewer remarked on the good literature review in the Discussion section.

DISCRETIONARY REVISIONS (WHICH THE AUTHOR CAN CHOOSE TO IGNORE)

Please list the contribution of each author.

Response:
As suggested by both the editor and the reviewer, this information has now been duly added.
Reviewer’s report
Title: Socio-economic class, rurality and risk of cutaneous melanoma by site and gender in Sweden.
Version: 1 Date: 6 August 2007
Reviewer: Carlos A Reyes Ortiz
Reviewer’s report:
General
This is a study on melanoma risk related to socioeconomic status (SES) -measured by occupation-, and town size (rurality) by site and gender in Sweden, and adjusted by geographical distribution and period of diagnosis, using registry data, and made by Perez-Gomez et al.
In general, it is a very well design study, well written and with important results. Authors discussed well potential explanations of their results, including some differences found between men and women probably related to job categories classification (or accuracy) as a potential limitation of their results.

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MAJOR COMPULSORY REVISIONS (THAT THE AUTHOR MUST RESPOND TO BEFORE A DECISION ON PUBLICATION CAN BE REACHED)
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MINOR ESSENTIAL REVISIONS (SUCH AS MISSING LABELS ON FIGURES, OR THE WRONG USE OF A TERM, WHICH THE AUTHOR CAN BE TRUSTED TO CORRECT)
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DISCRETIONARY REVISIONS (WHICH THE AUTHOR CAN CHOOSE TO IGNORE)
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What next?: Accept without revision
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.
Declaration of competing interests: I declare that I have no competing interests.

Response:
We should like to thank the reviewer for his time and his favourable view of our paper.
Reviewer's report

Title: Socio-economic class, rurality and risk of cutaneous melanoma by site and gender in Sweden.

Version: 1 Date: 1 August 2007

Reviewer: Elsebeth Lynge

Reviewer's report:

General

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**MAJOR COMPULSORY REVISIONS (THAT THE AUTHOR MUST RESPOND TO BEFORE A DECISION ON PUBLICATION CAN BE REACHED)**

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**MINOR ESSENTIAL REVISIONS (SUCH AS MISSING LABELS ON FIGURES, OR THE WRONG USE OF A TERM, WHICH THE AUTHOR CAN BE TRUSTED TO CORRECT)**

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**DISCRETIONARY REVISIONS (WHICH THE AUTHOR CAN CHOOSE TO IGNORE)**

Nicely written paper based on a large data base, good literature review in Discussion.

What next?: Accept after minor essential revisions

Level of interest: An article whose findings are important to those with closely related research interests

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

Response:

A professional English translator has corrected again the manuscript

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

Declaration of competing interests: I declare that I have no competing interests.

Response:

Here too, we should like to thank this reviewer for her time and her favourable opinion of our paper