Author's response to reviews

Title: The association between secondhand smoke and the risk of developing acute coronary syndromes, among non-smokers, under the presence of several cardiovascular risk factors: the CARDIO2000 case-control study

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PDF covering letter
To: Editor in Chief
BMC Public Health

Athens, April 20th, 2001

Dear Editor

We would like to thank you, once again, very much for the attention given to our article entitled “Passive Smoking And The Risk of Developing Acute Coronary Syndromes: The CARDIO2000 Study”. We read carefully the reviewers’ comments and we made an effort to address them with a more precise way. Moreover, we tried to correct several grammar and spelling errors that the reviewers mentioned. Thus, according to your suggestion, we re-resubmit a version of the manuscript and we kindly ask you to consider it for publication in the BMC Public Health Journal. Potential publication of our article, in the journal, would be a great honour for our study group.

All authors have read and approved the revised version of the manuscript. Furthermore, the authors state that the manuscript is not under consideration elsewhere and no conflict of interest exists. The Hellenic Heart Foundation grants CARDIO2000 project, as it is stated in the acknowledgements of the manuscript. Also, the Cardiology Department of Hippokration Hospital (School of Medicine, University
of Athens / National Health System, Ministry of Health) supported the coordination of this study. All authors have read and approved the re-submission of the manuscript.

We thank you for your time and consideration on our behalf.

With respect,

Demosthenes B Panagiotakos
Replies to Dr Malcolm Law comments (n = 1)

We would like to thank you very much for the attention given to our work.

<table>
<thead>
<tr>
<th>Comment 1</th>
<th>Check the manuscript for errors</th>
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<tbody>
<tr>
<td>Reply</td>
<td>We made an effort to correct the grammar and spelling errors in the manuscript.</td>
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</table>
Replies to Dr Stanton Glantz comments (n = 12)

We would like to thank you, once again very much, for your useful comments that helped us to improve, as we believe, the presentation of our work.

<table>
<thead>
<tr>
<th>Comment 1</th>
<th>Replace the terms environmental tobacco smoke or environmental smoke with “secondhand smoke” throughout the MS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reply</td>
<td>We followed your suggestion precisely</td>
</tr>
<tr>
<td>Comment 2</td>
<td>Last sentence of results needs clarification</td>
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<tr>
<td>Reply</td>
<td>We apologize for the confusion we made. You understood correctly that we tried to discuss the finding presented in Figure 1, but our English didn’t help us! We rephrased the sentence according to your suggestion as follows “Moreover, the previous risk increases progressively from 15% to 256% if one or more of the classical cardiovascular risk factors (i.e. hypertension, hypercholesterolemia, diabetes mellitus, sedentary life and family history of premature coronary heart disease) are present”.</td>
</tr>
<tr>
<td>Comment 3</td>
<td>Abstract…1st sentence of the conclusion: replace :other risk factors prevail” to “when other risk factors are present”</td>
</tr>
<tr>
<td>Reply</td>
<td>We followed your suggestion</td>
</tr>
<tr>
<td>Comment 4</td>
<td>Page 3, 1st paragraph…the intro needs to be focused on the things that are new about this study: the</td>
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</tbody>
</table>
relationship between passive smoking and ACS, the effects of relatively light exposures, and the interaction between passive smoking and other risk factors for ACS (see figure 1)

| Reply | We followed your suggestion, and we rephrased the first paragraph as follows: “However, the relationship between passive smoking and the development of acute coronary syndromes, especially in countries with high prevalence of active smoking, is not well studied. Moreover, the effects of relatively light exposures, the duration of the exposure, and the interaction between passive smoking and other risk factors related to cardiovascular disease, have rarely been investigated in the past”.
We thank you for this specific comment that we believe helped us to raise the point of our work. |
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<tbody>
<tr>
<td>Comment 5</td>
<td>Page 4…the use of + / - is ambiguous…</td>
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</table>
| Reply | Regarding the matching procedure, each control was in the interval

[age of the patient ± 3 years]

When we present the age of the patients and the controls we give mean value and SD (we clarify this in the manuscript). Moreover, you gave us another idea of a better presentation of the age distribution, i.e. to include the range of the age. |
Comment 6  |  Page 6, line 18…delete the words “by design”
Reply                  |  We deleted them

Comment 7  |  Page 7, line…in the exponential model of the effects of exposure time you are not including the effects of other risk factors or confounding variables…
          |  Present the quantitative results of this analysis in the results section.
Reply                  |  We applied exponential regression analysis to the data series \{time \{i, i+k\} of exposure, corresponding odds ratio, adjusted for all the potential confounders\}_L.
          |  Thus at each time interval we had the following points:

<table>
<thead>
<tr>
<th>Adjusted odds ratio for the same group of confounders</th>
<th>Time interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>OR₁</td>
<td>&lt;1 year</td>
</tr>
<tr>
<td>OR₂</td>
<td>1 to 4</td>
</tr>
<tr>
<td>OR₃ etc</td>
<td>5 to 9 etc</td>
</tr>
<tr>
<td>…</td>
<td>…</td>
</tr>
</tbody>
</table>

Then based on the sequence (OR, time interval) \∀ point we applied simple regression analysis since the potential confounding effect of the other risk factors has already been evaluated in the estimation of the ORs. This type of analysis could also be done by the use of interpolation analysis, but we believe that a 6th
degree polynomial lacks interpretation. We tried to clarify, briefly, this method in the statistical analysis section, and we believe that further clarification may confuse the readers of the journal. However, if you believe that we should add further details we are willing to do it.

Comment 8  Results first line…Given the high smoking prevalence in Greece, these exposure rates seem low

Reply  We wrote: 297 (35%) of the patients and 259 (24%) of the controls were defined as non-smokers passive smokers. The current smoking rate for adults in Greece (age 12 – 64) is 37.6%, according to the EUROPEAN STATUS REPORT 2001 (page 32, Annex 1.1). However, there is no information regarding the exposure to secondhand smoke, throughout the country. As a matter of fact this paper will be (?) the first report regarding passive smoking in Greece. Moreover, we believe that the observed, by this study, rates are in accordance to the active smoking prevalence in Greece and the habits of the population.

Comment 9  Page 8, end of line 3…change by to with

Reply  Done

Comment 10  Page 8, last 4 lines…these statements do not make any sense…

Reply  You are right and we felt embarrassed reading again
these sentences. What we aimed to say is that we studied separately secondhand smoke only at work (after taking into account that they are NOT exposed at home, conditional rule) or only at home (after taking into account that they are NOT exposed at work). Then we studied secondhand smoke both at work and home…

We changed these sentences to: “…the odds ratio of developing acute coronary syndromes was 1.97 (P-value = 0.0031) for the non-smokers who were regularly exposed, only, at work, while it was found 1.33 (P-value = 0.0021) for the non-smokers who were exposed, only, at home….”

<table>
<thead>
<tr>
<th>Comment 11</th>
<th>The effects of light exposure. Do these exposures tend to be in restaurants and bars?</th>
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<tbody>
<tr>
<td>Reply</td>
<td>We added this information in the text and in the abstract as you suggested. In the results section we write: “The majority of the patients (58%) and controls (72%) defined as occasionally exposed to second hand smoke said that these exposures where mainly in restaurants, cafeterias and bars”. We focused on this point in the 1st paragraph of the discussion and in the conclusion, but we do not feel that we have to discuss more the source of exposure, since we believe that exposure to secondhand smoke makes...</td>
</tr>
</tbody>
</table>
harm even it becomes from work, home, restaurants, bars or cafeterias…

Comment 12  
Limitation… high background exposures in Greece.  
The unexposed group is not really “unexposed”…

Reply  
We included the limitation you mentioned in the appropriate section (“Finally, the high prevalence of active smoking and the few, and usually override, restrictions on public smoking, in the investigated population, may bias our results towards the null and might underestimate our findings”).

However, it is difficult (impossible?) for us to correct for the background exposures within the investigated population (even we tried to discriminate the “unexposed” form the “exposed”), since we do not have accurate information regarding the level of background exposure or the adoption of the restrictions on public smoking, over the country.

We thank you once again for the attention given to our MS. Your experience and your comments helped us to improve, as we believe, the presentation of our work.