Author's response to reviews

Title: A case-crossover study of alcohol consumption, meals and the risk of road traffic crashes

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Author's response to reviews: see over
To the Editor of BMC Public Health

We would like to resubmit for publication on BMC Public Health our revised manuscript now entitled *A case-crossover study of alcohol consumption, meals and the risk of road traffic crashes.*

We are very thankful to the Associate Editor and the reviewers for their positive and constructive comments, which we hope to have understood and incorporated entirely.

Here follows the point-by-point list of responses to the reviewers’ concerns.

**Reviewer: Daniel C Vinson**

1. Some who study injury don’t like the term “accident,” saying it implies inevitability. I think it’s fine and will let the journal’s editors decide whether to keep or revise it.

   *Changed in “crash” throughout the paper as also requested by the other reviewer and by the editor*

2. Similarly, the term “odds ratio” might be preferred over “relative risk” because conditional logistic regression calculates the former, not the latter. But since it’s reasonable to assume the odds ratios are close approximations of relative risks, this is a only a quibble.

   *Done, throughout the manuscript and tables, as also requested by the other reviewer*

**Reviewer: Damian Rzeznikiewicz**

Major Compulsory Revisions

1. Page 6, Paragraph 2 – state how you estimated the RR because Logistic Regression yields ORs.

   *Changed to OR*

2. Page 8, lines 3 and 4 must be rephrased

   *Done*

3. Page 8, paragraph 2 – the RR calculated don’t yield the correct answers if calculated from table 2. Are the calculations different for a crossover study? Perhaps this should be sent for statistical consulting if unclear.

   *The calculation did not yield the correct answer probably because the reviewer made them as if they were independent observations. Because the observations are paired, the same methods apply as for matched-pair case-control studies, e.g. the McNemar estimate - the number of discordant pairs with exposed cases divided by the number of discordant pairs with unexposed cases. Doing so, in table 2, 24/18 yields correctly 1.33.*

4. Authors should show a result table for adjustments made by hour

   *We are not sure whether the reviewer would like just to see this table or have it included in the paper. We would prefer not to add it to the manuscript, because it is cumbersome and adds no significant information. Therefore, we put it at the end of this letter. If, however, the Associate Editor prefers that it appears in the paper, we are ready to send immediately upon request a version of the manuscript with such table*

5. Paragraph 5… certain subgroups…3 of the 5 subgroups presented that “were associated with a greater risk of accident” showed non significant results, therefore, this is clearly a case of over reporting. Only significant results should be shown in that section, and the statistics should be presented so one can see the magnitude of the results (in this case the confidence intervals are rather wide which tell quite a bit of the story)

   *We have revised the paragraph accordingly*

Minor Essential Revisions

1. Page 2, spacing is needed between CI and ml

   *Done*
Page 2, formatting must be kept constant – definition of abbreviations should be capitalized or not, but must be consistent.
Done

2. Page 3, abbreviation CC should be presented in the background section, after the first appearance of the term ‘case-crossover’.
Done

Page 3, in your background, you use ‘food’ and ‘meals’ # must pick one
Done

3. Page 3 - Methods section should read like this #
Drivers admitted to an Italian emergency room (ER) after RTAs in 2007 were interviewed about personal, vehicle, and accident characteristics as well as hourly patterns of driving, and alcohol and food intake in the 24 hours before the accident. The relative risk (RR) of an RTA was estimated through a case-crossover, matched pair interval approach. Alcohol and meal consumption 6 and 2 hours before the accident (case exposure window) were compared with exposures in earlier control windows of analogous length # sentence is awkward, should be restructured
Done, thank you

4. Line 2 of introduction on page 4, RTA should be RTAs, that in turn are by far the most common cause of – injury? Or injury and fatality? Or fatality? Should not be injury mortality.
We rephrased the sentence
Line 5 – should not be last years-# recent years.
Done

Line 5 and 6 – contribution and consumption of what?
The word alcohol has been added
Lines 7-10 should be rephrased and if possible cut into 2 different sentences.
Done

Line 10 – at a low consumption level
Done

2nd part of paragraph 3 in the introduction should be rephrased – unclear
Done, we hope it is clearer now

Line 2, 4th paragraph…cause sleepiness, which is an additional trigger of RTAs.
Done

Line 3# alcohol and meal consumption (not meals)
Done

Line 4 # driving periods? Why is emergency room capitalized?
Done

5. Methods – line 4 and 5, ‘if they were’ should only appear once# if they were >14, alive at the time of arrival, and proficient…
Done

Paragraph 2, line 5 – When possible…
Done

Line 6 – ethics committee? Does the committee have a formal name?
Done

Data Collection – line 1, instead of restricted, perhaps write ‘limited’
Done

Paragraph 2, line 3 – drinking and driving habits…not reported in this article
Done

Line 4 # …before the accident. Additionally, sleep was tracked in the 48 hours before the RTA.
Done

Line 5, the windows for alcohol and food were 6 and 2 hours respectively.
Done
6. Main findings, paragraph 2……..even at intake(. . .). This would most likely correspond to…

Done

Paragraph 3, lines 4-5# this would be consistent with a previous report but not with another.

(singular)

Done

7. Page 10, line 5… the first one we are aware of…

Done

Line 7, missing a period after ‘explained’

Done

Strengths and limitations

Line 5… time while driving should be ‘time while driving’

Done

8. Page 11

Line 1 – while allowing for a full 6 hours in the control period and 24 hours in the exposure period prior to the accident.

Done, slightly modified

Line 11 – drinking and driving (not driving and drinking)

Done

Line 12 – drinking and driving, eating and driving

Done

Line 17 – … intoxication, the interview may be impossible, an event that occurred…

Done

Line 20 – scaling-down of alcohol

Done

9. Page 12 – line 2 – memory is likely to be enhanced---source please

Done

Line 3 – in theory, recall bias should lead to an underreport of exposure during control windows and therefore result in an overestimation of the risks.

Conversely, if it caused…

Done

In conclusion should be indented

Done

Last line… However, one cannot dismiss the idea that it does so in…

Done

10. Table 2 – titles are not well formatted

Done

11. Table 3 – perhaps include the reference category in the table

Done

Discretionary Revisions

1. Page 6 – Statistical Analysis

Line 3 - “was chosen according to previous literature”# was chosen based on previous…

Done

Line 3 – Maclure and Mittelman is previous literature—change wording of sentence

Done

Line 5 – food intake—is it food or meal?

Done

Lines 5 and 6 – review how to use ‘respectively’ above

Done

Line 7 – window – singular

Done

Line 10-11 – run-on sentence
Towards the end of the first paragraph, the definitions of the windows get a little complex and wordy – authors must try to clarify

*These are difficult concepts to convey and we have rewritten this part many times. We changed it again and hope is more comprehensible now.*

2. Page 7, par 2 – Should read –the interaction between alcohol and meals was studied by introducing a product term of the 2 exposures in the model. In a further attempt to isolate the pure effects of meal intake from the possible modification by the effects of alcohol, an analysis comprised of only subjects that had not ….was performed.

*Done*

3. Results … 877 injured drivers arrived at the ER during our recruitment shifts.

*Done*

Thank you very much.

Best regards

Stefano Di Bartolomeo and the other authors of the paper.
Table 4. Odds Ratios (OR) and 95% confidence intervals (CI) for alcohol and food intake with mutual and time-of-day hourly adjustment.

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
<th>95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol consumption in the previous 6 hours</td>
<td>2.52</td>
<td>1.18-5.40</td>
</tr>
<tr>
<td>Meal intake in the previous 2 hours</td>
<td>0.85</td>
<td>0.38-1.90</td>
</tr>
<tr>
<td>Hour 00:00-00:59&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Hour 01:00-01:59&lt;sup&gt;a&lt;/sup&gt;</td>
<td>4.45</td>
<td>0.44-45.98</td>
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<tr>
<td>Hour 02:00-02:59&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.96</td>
<td>0.13-29.45</td>
</tr>
<tr>
<td>Hour 03:00-03:59&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.11e-06</td>
<td>0-∞</td>
</tr>
<tr>
<td>Hour 04:00-04:59&lt;sup&gt;a&lt;/sup&gt;</td>
<td>4.48</td>
<td>0.28-72.7</td>
</tr>
<tr>
<td>Hour 05:00-05:59&lt;sup&gt;a&lt;/sup&gt;</td>
<td>6.88</td>
<td>0.57-83.06</td>
</tr>
<tr>
<td>Hour 06:00-06:59&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.73</td>
<td>0.29-10.41</td>
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<tr>
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<td>2.97</td>
<td>0.53-16.47</td>
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<tr>
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<td>2.69</td>
<td>0.49-14.93</td>
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<tr>
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<td>6.60</td>
<td>1.17-37.33</td>
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<td>3.10</td>
<td>0.56-17.17</td>
</tr>
<tr>
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<td>4.49</td>
<td>0.77-26.12</td>
</tr>
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<td>Hour 12:00-12:59&lt;sup&gt;a&lt;/sup&gt;</td>
<td>4.57</td>
<td>0.75-27.87</td>
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<td>Hour 13:00-13:59&lt;sup&gt;a&lt;/sup&gt;</td>
<td>8.63</td>
<td>1.27-58.66</td>
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<tr>
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<td>4.11</td>
<td>0.64-26.59</td>
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<tr>
<td>Hour 15:00-15:59&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.14</td>
<td>1.63-79.72</td>
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<tr>
<td>Hour 16:00-16:59&lt;sup&gt;a&lt;/sup&gt;</td>
<td>5.18</td>
<td>0.95-28.36</td>
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<td>2.81</td>
<td>0.53-14.84</td>
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<td>0.44-14.19</td>
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<td>0.40-12.95</td>
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<td>0.10-4.70</td>
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<td>0.01-3.28</td>
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<td>1.90</td>
<td>0.26-13.98</td>
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<td>Hour 23:00-23:59&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.54</td>
<td>0.06-5.08</td>
</tr>
</tbody>
</table>

<sup>a</sup>: reference category is hour 00:00-00:59