Reviewer’s report

Title: Adverse Childhood Experiences are Associated with the Risk of Lung Cancer: A Prospective Cohort Study

Version: 1 Date: 9 July 2009

Reviewer: Mieke Joanna Jean Van Hemelrijck

Reviewer’s report:

This paper addressed an important topic since both exposure and outcome are highly preventable by public health interventions. However, some major revisions are necessary in order to make the paper more readable. Good luck with the revision!

Major Compulsory Revisions

Abstract

1. The result section needs more numbers in order to be self-explanatory to the reader. Please remove some of the last sentences and provide some extra numbers.

2. Based on the small number of lung cancer cases and the findings of the study, your conclusion is too strong. There might be an association.

Methods

1. The methods are clearly written, but way too long. There are too many different analyses included in your paper, which makes it very confusing for the reader. Consider taking out some of the analyses you have done (see also comments for results section) and focus more on those analyses that have an impact on the clinical relevance of your paper.

I would suggest that you drop the following analyses:

• Confidence interval functions
• Competing risks

In addition, shorten the overall methods section and maybe consider writing a methods appendix. This makes it much easier for the reader to understand your methods and if necessary the reader can find the details in the methods appendix. Your methods section should not be more than 2 pages (now there are 6!). I think you can drop the competing risk analysis (see also below) and just discuss this possibility in the discussion.

2. Given that smoking is a causal intermediate in the pathway between ACE and lung cancer (as you also mention in your methods section), I think it is impossible to assess the relation between ACE and lung cancer while adjusting for smoking. This biases your results and is incorrect.

In this scenario you can only study these associations separately:
ACE #Smoking # Lung cancer

This means that you can study the association between ACE and smoking, Smoking and Lung cancer, and ACE and lung cancer.

As written by Rothman and Greenland in “Modern Epidemiology”: “Any factor that represents a step in the causal chain between exposure and disease should not be treated as an extraneous confounding factor, but instead requires special treatment as an intermediate factor”.

I suggest you read more information on this topic and rethink your methods. Maybe there is a possibility of using time-dependent exposures and covariates?

Results

1. Please create a general “table 1” as available in all other publications on cohort studies. This is essential for an epidemiological paper! At the moment you describe way too much numeric information with words. Create a frequency/mean table that report values for instance ever and never smokers.

   Ever (N= xxx) Never (N= xxx)
   Mean number of ACE (Sd)
   Age
   Parental history of smoking
   SES
   Etc.

   This will allow you to reduce for instance the first paragraph of “Incident hospitalization with lung cancer during follow-up” to only one sentence because you can refer to a table. The same is true for the first paragraph of “Death from lung cancer during follow-up”.

2. Drop the graphs in figure 2, 4, and 5

3. Drop the sentence “A possible association remained between ACE Scores ...” in the section “Death from lung cancer during follow-up”. As you have said, it is a small number and so therefore not worth mentioning in the results section. In addition, explanation of results needs to be in the discussion section. If you want to, you can comment on this in the discussion section.

4. Add the findings with adjustment for baseline history of asthma, COPD, cancer, or TBC to the table in figure 5. It is much easier for the reader to find numbers in a table!

5. Premature death from lung cancer # this makes it less easy to follow your results section. Try to rewrite your results section so that it guides your reader from table to table. So first describe everything in table 2 (which is now still called figure 2), then table 4, and table 5. You only have small numbers and so re-analyzing is not always strengthening your findings. It gives an impression of searching for a method that can find some significant results. It would be good if
you delete the section “premature death from lc” and the “competing risk”
section. You could also add the information of premature death analyses to the
section on table 3.

6. Also, I am not convinced by the methodology you use to address the
phenomenon of competing risks. The methods section does not describe any
specific method (eg. Grays & Fine competing risk analysis?). If you want to show
the possibility of competing risks, you might want to consider a graph that shows
the cumulative incidence for lung cancer and death (other than lung cancer
death) by using a censor variable (0=no LC, no death, 1=LC, 2=non-LC death). Another possibility is just mentioning the possibility of competing risks in the
discussion section.

7. It is interesting to show AR%, however it would be good to make this
paragraph a bit shorter and more focussed.

Discussion

1. This is definitely an interesting subject. However, when reading through this
paper I get the feeling that this was written as part of a thesis. I think that a lot of
the paragraphs can be rewritten – shorter and more focussed. Also, the
discussion section needs to have a better organized structure:
   a. Summary of findings
   b. What is known about the topic so far?
   c. What do your findings add? How can you explain them
   d. Strengths and limitations
   e. Conclusion

• Minor Essential Revisions

Introduction

1. Please provide a reference for the first paragraph

2. The last sentence of the second paragraph (the epidemiological findings
parallel ...) is not completely clear. Please rephrase.

Results

3. ACEs and Smoking Behaviour: Consider rephrasing the second sentence as
this is not clear to the reader now (However, the overall prevalence of ...)

4. Premature death from lung cancer: on average need to be removed once from
sentence

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

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.