Author's response to reviews

Title: The association between ambient fine particulate matter and incident adenocarcinoma subtype of lung cancer.

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May 11, 2017 - Responses to Reviewers’ comments

Reviewer(s)’ Comments: 

Reviewer #2: I appreciated the Authors' answers to my comments. I think that some of the presented results are interesting and deserve to be published. However, the manuscript need some further revision.

Thank you for your valuable feedback and thoughtful questions. Responding to them has improved our manuscript.

1. p.4 rows 91-94 "Since prevalent…… using sensitivity analyses" : This sentence is more appropriately reported , though similarly, in the "study covariates" section. Please, delete the repetition sentence from this section.

Response #1: We have deleted the sentence.

2 p.7 Smoking variable.
a. I've understood that you have performed different analyses to take in account both the possible confounding and modifier effect of the smoking variable. Some clarification are needed:

- In the multivariable model you have used as smoking variable the 'nested covariate' (defined by smoking status, duration of exposure and number of cigarettes per day). While, to test the modifying effect of smoking you had dichotomized the variable in quit in last 10 years or quit >10 years or never smokers. Can you explain why you have chosen a different cut-off to dichotomize the smoking variable than the one used for the nested variable?

Response #2: We wanted to compare our findings with others and therefore the cut-off with quitting within the last 10 years vs. never smokers/quit10+ years ago, was chosen. This is the same as was used by the Nurses Health Study (Puett et al. 2014). That way we were able to directly compare with their study. We have added wording to explain this choice in lines 152 to 156.

In addition, we did subgroup analyses (see below) where we compared past smokers (e.g. irrespective of when they quit) with never smokers. Thus we feel we have adequately covered the possible effect modification by smoking.

Moreover, you have also considered the effect in ever (?) and never smokers separately. Who are ever smokers? Are you referring to former smokers (without difference in time by cessation)? If yes, please change "ever" with "past" smokers, in the text, consistently with the table 1. Ever smokers also include current smokers, that are not represented in your population study.

Response #3: This is a great comment. We have changed the manuscript and replaced “ever” smokers to “past” smokers.

b. p. 7 row 160. This sentence, on the effect found, should be moved to the results section.

Response #4: The sentence has been moved to the result section.

3. p. 8 Results section. It would be helpful if the authors could add, in Table 1, the p-values for any statistical test performed to compare the distribution of the variables in cases and controls. Please, add a column in the table.

Response #5: A column of p-values has been added to table one.

4. p. 9 row 195. Please delete "(Table 2, Model 1)", reported again at row 197.

Response #6: We have deleted this as recommended.

5. p. 9 rows 206-209: Please replace "ever" with "past" (see point 2)

Response #7: We have replaced the “ever” with “past” throughout the manuscript.

6. Discussion.
a. p. 12 In my opinion, the authors should not focus too much the attention on the sensitivity analysis performed, for the reasons discussed in the first revision of this paper. So, I suggest to remove the title "Exclusion of prevalent Non-melanoma skin cancer" (row 160).

Response #8: We have removed the title.

Also, from row 282 to row 293 (p. 13) the authors discuss in this subsection the effect of ozone, but this should be a general comment and not related to NMSC exclusion.

Response #9: This is an important observation and we have moved this sentence to the Results section, line 193-195.

b. rows 265-266: Please delete the sentence "The rest of the studies… or not".

Response #10: We have deleted the sentence.

c. row 274: Please, use the acronym BCC, already defined, for basal-cell carcinoma

Response #11: We have fixed the sentence.

d. As already recommended, the authors should try to imagine a possible scenario to explain the result of this sensitivity analysis. Perhaps starting from a DAG, as suggested by the first reviewer, they should discuss the complicated relationship that seems to exist between NMSC, sun exposure, time spent outside, exposure to air pollutants and likely other uncontrolled factors (lifestyle, diet ...).

If authors think it is not necessary to use a DAG, I strongly recommend to add a sentence in the discussion trying to explain this relationship, as it is the innovative aspect of their work, as the authors have also pointed out in their conclusions.

Response #12: We agree that the observed effect modification of NMSC on the association between ambient PM and lung AC is unclear and needs to first be confirmed in other large cohort studies. Secondly, a plausible biologic pathway must be identified. Because this is the first observation of this possible relationship, we decided not to use a DAG diagram at this stage. However, we have added some sentences addressing the complexity of this finding (lines 282-295)