Reviewer’s report

Title: Annual decline in forced expiratory volume and airway inflammatory cells and mediators in a general population-based sample

Version: 1 Date: 31 Jul 2018

Reviewer: Olaf Holz

Reviewer's report:

The authors revised the manuscript and responded adequately to most reviewer comments.

1. As noted by all reviewers there were numerous mistakes and "typos" in the table of the original manuscript. Unfortunately there are still mistakes in the revised versions of the tables.

In table 2 the n numbers for the tertiles were corrected. But these corrected values do not match with the respective numbers in table 3. Which set of values is correct?

While the textile numbers were corrected the authors failed to proofread depending numbers in the table, such as male % (10 of 20 total is not 53%).

Please proofread all data and provide corrected tables.

In addition, there should be a note to table 2 that the mean Packyear level is derived from both current and former smokers and indicated in the comment to OH.

Please also provide a line that indicates the number of sputum samples that were available for the 3 tertiles. As indicated in comment CF3 and on page 9, line 12,13 "some" samples failed to fulfill the criterion of having 20% squamous cells. Please also delete "some" and state the exact number in the text.

2. The answer to comment OH8 is not clear

"4. The description of sputum induction is not clear. All participants inhaled first 0.9% and all participants then inhaled 3, 4, and 5%? Each inhalation period lasted for 7 minutes? The statement "until a sufficient amount was delivered" suggests that some subject only e.g. inhaled for 5 min others e.g. for 20 min. The danger in doing so is, that it could affect sputum composition, as the first portions produced are generally rich in neutrophils and later portions richer in macrophages."
Author's reply: Duration of inhalation was different in different participants and we used the whole expectorate excluding saliva prior. However, we have not noted how much NaCl concentration each patient needed.

Apparently, the total inhalation time was not standardized, which is likely to have increased the variability of sputum neutrophil counts. This cannot be corrected at this stage and is already described sufficiently in the method part.

For the reader it is not clear, if whole expectorate was processed (by definition this is unselected sputum containing large quantities of saliva) or if sputum was selected from saliva before the processing. The response to this question is not clear:

OH9"5. Was the sputum selected from saliva prior to processing? Or was the whole expectorate processed. This is important to interpret the biomarker levels in the supernatant."

Author's reply: Sputum was selected from the prior saliva. We have removed the excess sputum from the sample.

I figure that sputum plugs were selected, but then this needs to be clearly stated in the text. Using a criterion of maximal 20% squamous cells as indicated in the comment to CF3 is very strict and would we rather incompatible with using the "whole expectorate" for processing.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

No

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

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