Reviewer's report

Title: Lung function changes from childhood to adolescence: a seven-year follow-up study

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Reviewer: Erica Schultz

Reviewer's report:

Review of manuscript "Lung function changes from childhood to adolescence: a seven-year follow-up study" by Piccioni and colleagues.

This is an interesting study by Pavilio Piccioni and colleagues where they assess the lung function development from childhood to adolescence in relation to different “asthma classes”. In addition the authors aimed at comparing the spirometry values retrieved in this study with reference values obtained from Global Lung function Initiative 2012 reference equation. The study has some strength, with one being the early lung function measurement (at 4.5 years) as a baseline measure. The manuscript however, needs major revisions to make the research behind the manuscript more transparent.

Reviewer's report

- Major Compulsory Revisions

1. The Abstract section needs to be rewritten and follow a logic order.
   As it is now:
   Aim: Assess development in lung function and impact of persistent asthma.
   Verify GLI reference values
   Method: No description of how to GLI is verified.
   Results: Descriptive statistic of Asthma-Like-symptoms (ALS), no mention of persistent asthma. Please be consistent in which terms you use.
   Conclusion: The GLI is valid. Where is the result behind this statement?

   Please present numbers in abstract, and not just “significantly smaller”

2. The BACKGROUND section lacks focus on the topic. There is too much peripheral information. The authors have to focus the reader’s attention to the aims of the investigation. In addition please provide sufficient background information to motivate the choice of aims.

3. Please clarify which exposure definitions that have been used. In method section (line 117-121) the authors write about ALS. It is somewhat unclear what is used in this manuscript. Is it any (or maybe more than x times) ALS at
current/previous 12 months/since last follow-up or maybe a combination of ALS and/or clinically diagnosed asthma (also which time frame).

Line 142-144: Here is the definition of ALS. What the statement “In these analyses” refers to is unclear. Is ALS defined in any other way in some other analyses?

Limit definition of ALS to one section in the manuscript.

4. Line 147-151: “To compare the results of functional test, GLI reference values were calculated using GLI software….” It is unclear what the authors are comparing here. This section describes the calculation of GLI-ref values, but it would be beneficial with an explanation of how GLI-ref values are compared with those measured. Please clarify how this comparison is done. Please define when data is fitting the reference equation.

5. Table 3 & table 4 (as well as line 172-176): Please revise numbers or clarify. For example, look in table 4, for FEV1 and no symptoms: A mean delta change/yr of 181.9 ml. Should then this be the same as seen in table 3 for FEV1 for the Observed mean? But this is 233.4 ml.

6. Table 4 (line 181-182): Unclear how comparisons between groups were made. No symptoms as a reference?

7. Line 185: The authors state that asthma groups have less increase of FEV1/FVC over time. This is contradictory since not only do they show negative values in the Table 4, but also since FEV1 would be very close to FVC at 4 years of age and there should be an expected decline of the ratio over time in all subjects. This section needs to be rewritten and clarified.

8. Please add a section on potential limitations. FEV1, is it really suitable to use in 4 year olds? Small sample size, particularly in each ALS strata. ALS definitions - risk of misclassification? Residual confounding?

- Minor Essential Revisions

9. Line 32: Consistent or Concordant? They are synonyms.

10. Line 130: Spirometry testing was performed in a similar manner 2010 (not 2003).

11. Line 134: Please clarify in brief what the exclusion criteria from 2003 are. (Interesting as they are local and in so young children) Where there any repeatability criteria for exclusion?

12. Tables: Please check author instructions for abbreviations and footnotes to complete tables.

13. The number 1 in FEV1 should be subscript. Please check in whole manuscript. (The same for FEV0.5 etc)

14. Line 151: When appropriate? Please clarify?
- Discretionary Revisions

15. Line 5: Check the numbers of affiliations. P.Piccioni has a number 2?

16. Abstract: Line 28-29 Confusing with having the words “environmental pollution” in abstract, as the authors are not investigating this.

17. A flow-chart of the study population, where the authors clearly state the reasons for exclusion would be beneficial.

18. Line 99: Please check the numbers. (In ref 5, I can’t find the 1005 subjects anywhere), in addition it seems like the age span in ref 5 is 3-6 years and not 4-5 years.

19. It would be interesting to see some sensitivity analyses of those treated vs not. Maybe there is some misclassification of early transient ALS, because of successful treatment. Do you have this information?

20. Table 3: This table might benefit from being presented in z-score.

21. Figure 1: The “horizontal” line between the different ALS groups makes the figure unclear. The impression is now that the same individuals are followed over time, but there is no time on x-axis and there are different individuals in each ALS-group. Otherwise a nice and clear figure.


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

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

Coauthor of a submitted paper with similar topic as this manuscript.