**Author's response to reviews**

**Title:** Relationship between daily physical activity and aerobic fitness in adults with cystic fibrosis

**Authors:**

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**Version:** 3  
**Date:** 4 April 2015

**Author's response to reviews:** see over
Cover letter

To:
The Editors of *BMC Pulmonary Medicine*

Dear Dr. Sanjay Chotirmall,

Please find enclosed the manuscript entitled “Relationship between daily physical activity and aerobic fitness in adults with cystic fibrosis” by authors Savi D, Di Paolo M, Simmonds N, Onorati P, Internullo M, Quattrucci S, Banya W, Laveneziana P, Palange P.

Thank you for the decision to accept our manuscript. We have taken into account all the comments and a full description of our responses to reviewers comment is also attached.

EDITORIAL REQUEST:

1. Clarify in the manuscript if consent was written and informed.

**Answer:** Thank you. Yes, we have specified in the Methods that the consent was written and informed. The sentence was changed as suggested by the editor as followed: “All subjects provided written informed consent.” (Study design, page 4 lines 23-24).

2. Details of any funding to be included in the Acknowledgements

**Answer:** Thank you. We don’t have any details of founding related to this study to be included in the Acknowledgements. We would like to thank the “Lega Italiana Fibrosi Cistica-Associazione Laziale Onlus” for the support of the Hospital Cystic Fibrosis Center.

**Reviewer 1:**

**Reviewer's report**

**Title:** Relationship between daily physical activity and aerobic fitness in adults with cystic fibrosis

**Version:** 2 **Date:** 10 February 2015
Reviewer: Bradley Quon

Reviewer's report:

Major Revisions:
These have been adequately addressed by the authors.

Discretionary Revisions:

The authors may consider rewording the discussion of the sample size calculation as well. Specifically the phrases "total 36 subject" (total OF 36 subjects?) and "estimation of the calculation" (remove "estimation of"?"

Answer: Thank you. We rewrote the discussion of the sample size calculation as suggested by the reviewer as follows: "The calculation for sample size was done using a previous study by Troosters et al. [15] who showed a difference in V'O$_2$ peak % predicted of 41 with a standard deviation of 13.62. We proposed that our effect size could be about half of that obtained by Troosters et al. [15], therefore for 80% power and 5% significance and similar variability it would require a total of 36 subjects in a ratio of 2:1. We therefore recruited 45 in total in a ratio of 2:1".

Study design, page 5 lines 10-15.

Level of interest: An article of importance in its field

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

Reviewer 2:

Reviewer's report

Title: Relationship between daily physical activity and aerobic fitness in adults with cystic fibrosis

Version: 2 Date: 15 February 2015

Reviewer: Theodore Dassios

Reviewer's report:
The authors have provided a very good revision addressing all remarks initially raised on the first version of this manuscript. They took the time and effort to go back and recruit new patients and enrich their study group and for this they are
commendable. I have no other outstanding concerns with regards to this manuscript.

**Answer:** Thank you.

**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.

**Reviewer 3**

**Reviewer's report**

**Title:** Relationship between daily physical activity and aerobic fitness in adults with cystic fibrosis

**Version:** 2

**Date:** 16 February 2015

**Reviewer:** Michelle Murray

**Reviewer's report:**
This resubmission seems to have addressed the main concerns of the reviewers and acknowledges its limitations with respect to sample size and control numbers. They have amended the manuscript accordingly.

**Answer:** Thank you.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

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

**Declaration of competing interests:**
I declare that I have no competing interests

**Reviewer 4**

**Reviewer's report**

**Title:** Relationship between daily physical activity and aerobic fitness in adults with cystic fibrosis
Reviewer: Narelle Cox

Reviewer's report:
In this paper the authors identify the inherent difficulties associated with assessing exercise capacity using formal CPET measures, and highlight the possibility of daily physical activity monitoring serving as a marker for submaximal exercise intensity. The paper has been substantially re-written and its readability much improved.

Major Compulsory
Nil

Answer: Thank you.

Minor Essential
1- In the text (page 11, line 5) correct spelling of author name to Hebestreit.

Answer: Thank you. Done

2- In “Statistical analysis” (page 7, line 11 and 19) the abbreviation for interquartile range (IQR) appears before the full description of the term.

Answer: Thank you. We rewrote the sentence for clarity as suggested by the reviewer and the abbreviation for interquartile range (IQR) appears after the full description of the term. The sentence was changed as followed: “non-normal numeric data were presented as median (interquartile range, IQR)”. Statistical analysis, page 7 lines 10-11.

3- Results (Page 8, line 21) please clarify the MET value above which is considered moderate intensity – ie. Change to 4.8 METS to reflect earlier note that definitions for MET activity levels are the same as those reported by Troosters et al.

Answer: Thank you. In this study the time spent at 4.8-7.2 METS was considered “moderate” activity. So, we have clarified the METS value as suggested by the reviewer and the sentence was changed as followed: “PA of moderate (4.8-7.2 METS) intensity was related to VO\textsubscript{2} uptake at LT”. Results, page 8 line 21.

4- Results (Page 8, Line 22-23) recommend insert a comma after moderate and after the close bracket – alternatively indicate that moderate to vigorous physical activity intensity would be anything greater than 4.8 METS.

Answer: Thank you. As suggested by the reviewer, we rewrote the sentence as followed: “Physical activities above the threshold of moderate (4.8-7.2 METS) and vigorous (>7.2 METS) intensity were also related to VO\textsubscript{2} uptake at LT”. Results page 8, lines 23-24.

5- Discussion (Page 11, line 13) change prevent to prevents
Answer: Thank you. Done

6- Discussion (Page 13, line 12) change affects to affect

Answer: Thank you. Done

Discretionary

1- Discussion (page 11, line 20-24) – in the comparison of your physical activity findings relative to Ward et al – it would be good to postulate why your population recorded around 30 mins per day less moderate intensity physical activity than the participants in the Ward et al study eg. Effect of difference in recording period/gender make up of participant groups/ season of year during data collection etc.

Answer: Thank you. The sample of Ward et al. recorded a mean of 43 min of moderate physical activity at one month post-discharge, considerably greater than the 14.8 min reported by Troosters et al., the 14 minutes reported by Van Remoortel et al. and finally considerably greater than the 13 min reported by our study. On the other hand, our findings are comparable to those of Troosters et al. and to Van Remoortel et al. for times spent in moderate physical activity (13 minutes in our study vs. 14.8 reported by Troosters et al. and 14 minutes reported by Van Remoortel).

Ward et al. wrote in their discussion that this finding is surprising, particularly since their sample were still recovering from an acute exacerbation and one would therefore have hypothesized that they would be less active.

So, the reason for this discrepancy in results between Ward et al. who reported a mean of 43 min of moderate physical activity and our results is not clear, especially because our results are in line with the present literature (Troosters et al. and Van Remoortel et al.).

It is possible that differences in physical activity results may reflect cultural differences, patients’ motivation to participate in the study, a small sample size or a sampling error.

Larger studies may be needed to objectively confirm the physical activity levels in adults with CF.

2- Discussion (page 13, line 13) – the sentence “Finally, our CF patients’ peak symptom limited VO2……) lacks context here. It might benefit from an additional sentence for clarification.

Answer: Thank you. We agreed with the reviewer and we wrote an additional sentence for clarification as followed:” Finally, our measurements at peak exercise revealed that CF patients’ peak symptom-limited V'O₂ was reduced by 24% of the predicted normal value and that there were no differences between the CF and the healthy group in the V'O₂/work rate slopes which were within the normal range.” Discussion, page 13, lines 14-17.

3- Discussion (page 13, line 16) consider changing “several” to “other”,
alternatively, give an example of the types of factors which may contribute to reduced exercise tolerance but which you haven’t investigated.

**Answer:** Thank you. We agreed with the reviewer and we changed “several” to “other”. Discussion, page 13, line 18.

4- Discussion (page 13, line 21)- possibly clarify, compared to whom, your healthy controls are more sedentary than.

**Answer:** Thank you. We wrote that our healthy control group seems to be more sedentary than Troosters’s control group because we have the levels of physical activity of both groups and we can appreciate the differences. Discussion, page 12 lines 6-8.

Regarding the limitations of the present study (page 13, lines 23-26) we can only say that our healthy controls are disease-free but possibly “sedentary”, so we have removed the term “more” from the text. Page 13, line 23.

**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

We finally inform you that:

- the present manuscript, or part of it, has neither been published nor is currently under consideration for publication by any other journal.
- Pierantonio Laveneziana and Paolo Palange have equally contributed to the manuscript and are both last authors.
- Daniela Savi is a PhD fellow in “Biotechnology applied to Clinical Medicine”, Sapienza University of Rome, Rome, Italy.

Kind regards,
Dr. Daniela Savi