Reviewer’s report

Title: Circadian rhythm of COPD symptoms in clinically based phenotypes. Results from the STORICO Italian observational study.

Version: 0 Date: 30 Apr 2019

Reviewer: Marise Kasteleyn

Reviewer's report:

General:

Interesting topic. However, the main outcome/research question is not so clear. The methods should be rewritten so that the primary aim is more clear, and methods including analyses should be in line with that aim. Also, since many tests are performed it is difficult to distinguish main and side issues. Also, in the discussion all those secondary tests are not discussed, so for me it is not clear what the added value of these analyses is. Also, there are several language errors, so an English check is recommended.

Introduction:

- Recent interesting ACOS study definition https://www.ncbi.nlm.nih.gov/pubmed/28461292

- Rationale for evaluating circadian rhythm is missing. And why do you expect differences between those phenotypes regarding the circadian rhythm.

- “whereas” seems the wrong word in line 42, it is not in contrast with the statement before the comma.

- Results that are reported in abstract are not reported in body of article (eg regarding CM patients being more commonly overweight etc). Focus should be on main findings in abstract.

Methods:

- Longitudinal study, but the current study seems a cross-sectional analysis. That should be more clear in design.

- Many outcomes are included. Why so many?
Please provide more information about the Night-time, morning and day-time symptoms of COPD questionnaire. This is an important outcomes, but details (eg about scoring) are missing).

IN the statistical analyses it is stated "main outcomes" are dyspnea, HR-QoL, etc". IN my opinion, the main outcome should be circadian symptoms.

Results:
- Full titles of figures do not need to be reported in the text.
- What is considered a satisfactory score? How do you know > 6 is satisfactory?
- Figure 2 and 3 is of low quality and difficult to read/not readable.
- Footnotes are missing in the table to explain abbreviations
- It is indicated that proportion of subjects with night time subjects was higher in the CB group compared to other groups. I suggest to perform statistical analysis to test this difference, but write in the limitation that this should be interpreted with caution.
- The paragraph on line 213-224 is really difficult to read, given all the numbers and different tests.
- In the methods it is stated that IPAQ is reported both continuous and categorical, but in table 3 only the categorical results are reported. What about the continuous outcome?
- Regarding the differences between phenotypes in Qol, sleep, mood and physical activity it would be helpful to have the exact numbers as well, instead of only p-values,
- Why did the authors choose to dichotomize the symptoms? Why not use continuous variables?

Discussion:
- Main finding is clearly stated. However, it was not tested whether this differences was statistically significant, nor there is any discussion regarding whether this is clinically relevant.
- See also literature of van Buul et al. about morning symptoms and physical activity over the day in COPD patients

- Please do not repeat exact number in discussion
- It is recommended to assess nocturnal symptoms, but what should we do if we are aware of the presence of those symptoms?
- First sentence of conclusion is not so clear and not in line with study findings.

**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.

No

**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.

I am able to assess the statistics

**Quality of written English**
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

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