Author’s response to reviews

Title: Measuring health-related quality of life in chronic obstructive pulmonary disease: properties of the EQ-5D-5L and PROMIS-43 Short Form

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Author’s response to reviews: see over
Dear Editor,

This letter accompanies the manuscript entitled “Measuring health-related quality of life in COPD: properties of the EQ-5D-5L and PROMIS-43 Short Form” which we have revised for reconsideration for publication in BMC Medical Research Methodology (manuscript number: 1940461120118522). We are grateful to the reviewers for their thoughtful comments and appreciate the opportunity to revise and resubmit the paper. We have responded to each of the reviewer comments in the pages that follow, and have indicated the changes made to the manuscript to address the Reviewers’ concerns.

All authors have approved of the revised manuscript. We appreciate the opportunity to be reconsidered by BMC Medical Research Methodology. Thank you in advance for your time and your consideration.

Sincerely,

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RESPONSE TO REVIEWERS: Review of “Measuring health-related quality of life in chronic obstructive pulmonary disease: properties of the EQ-5D-5L and PROMIS-43 Short Form”

We thank the Reviewers for the comments about our work and for the thoughtful review of the original version of this manuscript. In the paragraphs below, we have responded to the Reviewer’s comments and we have indicated, where appropriate, the specific changes made in the manuscript to address the noted concerns.

Reviewer 1: Nan Luo

Major Compulsory Revisions: The conclusion is not accurate as the reliability of the EQ-5D-5L was not assessed.

RESPONSE: We have dropped the mention of reliability in the conclusion.

Reviewer 2: Renee Stark

Major compulsory revisions:

Methods:

1. Patient selection: why were only patients aged 40 or older included? While the other inclusion criteria were self-explanatory, it would be useful to the reader if this criterion was briefly explained.

RESPONSE: We added the explanation and reference following the age criteria “≥40 years of age (as COPD mainly affects people over the age of 40 and the disease develops over decades of exposure to inhaled particulates (Buist et al, 2007)” (Method section on page 5).

2. For the correlations, the authors should consider using spearman rank correlation. Since the EQ-5D Levels for each dimension would be considered as ordinal (Table 4) and the mMRC dyspnea scale is also ordinal (Table 5), this would support the use of the spearman correlation and would be unlikely to have any disadvantages.

RESPONSE: We agree, and have changed all of the correlations to Spearman’s rank correlation coefficients (Table 4 and 5), which did not substantially alter any of the results. Data presented in text of Results were revised as well.

Results:

1. Table 1 describes the baseline characteristics. Of importance would also be a description of cardiovascular comorbidities, especially since they are also associated with smoking. The authors perhaps planned to include this, since they included in the notes “**Include angina, coronary artery disease …” but did not have a corresponding row in the table.
RESPONSE: We apologize, this information was reported in a previous draft, and we now include comorbidities in Table 1. We also revised the associated text in the 1st paragraph of Results: “Patients included as GOLD 3 and 4 (with more severe disease) were significantly younger, more likely to be African-American, have a lower education level, less household income, a heavier smoking history (p<0.05), and less likely to have coronary heart disease, as compared to those with mild to moderate disease (Table 1).”

2. According to Table 1, there are significant differences between the GOLD classification levels 1,2 versus 3,4 regarding age, race, education, household income and mean smoked pack-years. The authors should consider whether these factors could be confounders for the observed differences in the clinical and HRQL measurements (Table 3). Usually in observational studies, one would adjust for significant differences between the groups (GOLD category) by using a regression model, and it would seem appropriate to at least adjust for age and sex. Furthermore, in the EQ-5D and the EQ-VAS increasing age has a negative effect on the values, i.e., with increasing age EQ-5D and VAS tend to decrease, thus in the case of this population, age may have a confounding effect since the patients in the highest GOLD category also have the lowest mean age and thus the differences may be reduced due to the effects of age (see EQ-5D user manual).

RESPONSE: Acting upon the reviewer’s suggestion, we ran an analysis of covariance (ANCOVA) to adjust for age as a confounder. The results did not significantly change. We noted this additional analysis by adding the following text in the last paragraph of Discussion: “Age is a known factor that could confound the association between HRQL and disease severity (Stahl et al, 2005). In order to rule out the confounding effect, we also conducted an analysis of covariance (ANCOVA) to control for age when comparing the responses in EQ-5D, PROMIS domain scores, dyspnea measures, and 6MWD among patients with different GOLD grades (data not shown). Similar results (F-statistic and significance level) were found as in Table 3 after controlling for age effect, except that the discriminative ability of 6MWD and PROMIS sleep disturbance (P-SD) to distinguish COPD patients of different severity was improved.”

3. Table 3: the use of RE ratio is an interesting concept – could the authors please provide a reference for this. Furthermore, the authors should comment whether it is possible to compare the F-statistic from different anovas especially considering that the variability of the different measures of dyspnea will be different e.g. mMRC varies from 0 to 4 whereas Borg dyspnea scale varies from 0 to 10 and FACIT and the PROMIS subscales are transformed using the T-score metric. This difference in scales could be overcome by standardizing the different values to a mean of 0 and standard deviation of 0 using proc standard in SAS.

RESPONSE: Thank you for the comment, we have cited the use of RE from several publications. Since F-statistics are the ratio of explained and unexplained variance (or the ratio of between-group and within-group variability), the scale of the dependent variable would not impact the magnitude of F-statistics and therefore it is not necessary to standardize the metric for each measure in order to take ratios of F-statistics.

Minor essential revisions:
Table 3: definition of FEV1 is included in the notes at the bottom of the table, however this abbreviation is not used in the table. Either the authors should include this information in the table or delete this abbreviation.

RESPONSE: We have deleted the FEV1 definition in the table footnote.