Author's response to reviews

Title: Disease knowledge level is a noteworthy determinant of anxiety and depression in patients with Chronic Obstructive Pulmonary Disease: a cross-sectional studies

Authors:

Qiao Zhang (zhangqiaoo@gmail.com)
Jiangrong Liao (liaojiangrong@yeah.net)
Xiuqing Liao (XQ_Liao@126.com)
Xiuling Wu (xl_wu2001@163.com)
Min Wan (W_an521@sina.com)
Changzheng Wang (czwang@yeah.net)
Qianli Ma (cqmql@163.com)

Version: 3
Date: 7 April 2014

Author's response to reviews:

Dear Editor,

Thank you very much for your constructive comments on our manuscript, MS: 1299139599118339. We have carefully read the comments from referees and revised our manuscript accordingly. Listed below please find our point-by-point answers in response to the concerns of reviewers.

Referee 1:
Thank you for the comments for promoting our revision of more information and clarification about our study's design advantage.

Major Compulsory Revisions

1. General comment: The central premise of the study/article is identification of determinants of anxiety and depression in patients with COPD, and this term is used throughout the manuscript. However, “determinant” implies a causal relationship, and this is a cross-sectional study. This may be an artifact of language, but the most this study can do is identify factors associated with anxiety and depression in these patients. This confusion and mis-use of the word “determinant” exists throughout the manuscript (including Background) and should be clarified.

Answer: Thanks for the comment. In this paper, “determinant” was used as being a risk factor of anxiety and depression in COPD patients, and they were described in http://en.wikipedia.org/wiki/Risk_factor, in which pointed out “Risk factors or determinants are correlational and not necessarily causal…”. Also, “determinant” was used frequently in published studies (reference 1,2,9,10). So we hope keep this expression.

2. General comment: “Interventional” is also a term used throughout the
manuscript. It is presumed to refer to an area where intervention could have an effect on outcome, but in areas where an efficacious intervention has not been demonstrated in the literature, the authors may wish to acknowledge that (e.g., “possible intervention” or “intervention opportunity”).

Answer: As suggested. We have changed “Interventional” to “addressed” or “possible interventional” or “possible targeted” for the more appropriate expression throughout the paper.

3. Background: The authors do not propose hypotheses that they then test with data. Thus, the mechanism by which low levels of disease knowledge would result in anxiety and depression is not presented. Instead, they seem to have collected data on a number of variables and then analyzed all of them. It would be interesting to know what variables the authors hypothesized would be significantly associated with anxiety and depression (including the sub domains of the COPD knowledge measure). (These concerns also apply to the Statistical Analysis and Results sections.)

Answer: Thanks for the comment. Firstly, in paragraph 2, 3 of Background, we had described the hypotheses. #The other researchers' have found that “Anxiety and/or depression symptoms of COPD patients were improved by pulmonary rehabilitation[11-13]. Patients' education, as the necessary element of pulmonary rehabilitation, is related to improving COPD patients' disease knowledge level[14]”, that is mean that the relief of anxiety and depression symptoms may be related to patients' education addressing COPD patients' disease knowledge level. # And then, we showed our previous result that “the COPD patients with more disease knowledge had fewer symptoms of anxiety and/or depression in our COPD management plan”. So we proposed the hypotheses that “COPD patients' disease knowledge plays the important role in improving anxiety/depression”, and tried to find out the possible targeted key topics of the COPD knowledge in 13 topics of The Bristol COPD Knowledge Questionnaire (BCKQ). Both of statistical analysis and results sections were focus on the above goals in this paper.

Secondly, as mentioned before, the key target of this study was “COPD patients' disease knowledge plays the important role in improving anxiety/depression”. Only the hypotheses had been proved, the mechanism of this determinant became another scientific question.

Thirdly, we analyzed most risk factors found by other researchers and ours together. This was the advantage of our study's design. Then we could measures the degree of association between the COPD patients' disease knowledge level and anxiety and depression in patients with COPD, with the effect of other risk factors removed. For example, in Result/Correlation of HAD Total Score with Characteristics of Subjects, para.2, Spearman correlation analysis revealed most variables were significant correlation with the HAD total score, once we removed the effect of other factors (the partial correlation analysis), just 4 risk factors revealed significant correlation with the HAD total score.

Fourthly, what the sub domains of the COPD knowledge measure would be significantly associated with anxiety and depression exactly is what we expect
through the data analysis results. In the fields, little research had been carried out. So we had to explore the correlation between any possible sub domains and anxiety/depression in COPD patients.

4. Background, para. 1: Anxiety and depression can have deleterious effects on physical disability and morbidity, but the impact is bidirectional, and this should be acknowledged (i.e., people with high levels of physical disability and morbidity can become depressed as a result).

Answer: Thanks for the comment. There is no doubt that anxiety and depression can have bidirectional effects on physical disability and morbidity. However, in Background, para.1, we just provided the attention to the negative effects of anxiety and depression in COPD patients, rather than the risk factors leading to anxiety and depression of COPD patients. In fact, the issue was referred in Background, para.2.

5. Background, para. 2: This paragraph is confusing and incorrect. In addition, the authors seem to suggest that interventions to improve anxiety and depression need to be indirect (e.g., through education, pulmonary rehabilitation) rather than directly through psychological/psychosocial interventions. This does not negate the possibility of achieving improvements in anxiety and depression levels through other means, but successful psychological/psychiatric interventions to address anxiety and depression should be acknowledged.

Answer: Thanks for the comment. It is very sorry to cause your confusion. In Background, para.2, you can find that we didn’t analyzed the ways of the treatment of anxiety and depression, however, in this section, the risk factors were mentioned, and most of these factors were found that were difficult to be addressed (such as gender, age, etc.). There were only two possible risk factors confirmed by two indirect methods. Because COPD knowledge was contained in these methods, it is content to predict that “COPD patients' disease knowledge plays the important role in improving anxiety/depression”.

6. Background, para. 3: It would be helpful if the authors would clarify when they are referring to general educational level and disease-specific education.

Answer: Thanks for the comment. Firstly, in Background, para.3, we didn’t mention "Disease-specific education " and "general educational level". Only the "COPD patients' disease knowledge level" was mentioned in the paragraph. Secondly, the COPD patients' education related COPD knowledge can be understood as "diseases - specific education". It is clearly different from "general educational level". So it should not cause confusion.

7. Methods/Participants and Measurements, para. 1: There was no mention as to whether any of the participants in this study were receiving treatment for their anxiety and depression at the time of the assessment.

Answer: Thanks for the comment. We collected comorbidities and concomitant therapy of these subjects. None of these subjects were receiving treatment for their anxiety and depression at the time of the assessment. So we didn’t mention in the manuscript. As suggested, we added the information (Result/Characteristics of Subjects, para.2, line7-8).
Methods/Participants and Measurements, para. 1: How, when and where were patients approached, consented and assessed? How many refused participation and for what reasons? How did they complete the measures (e.g., paper and pencil, computer, interview)?

Answer: Thanks for the comment. In Methods/Participants and Measurements, para.1, the first sentence has pointed out the information. As suggested, we added the information about how they completed the measures in Methods/Participants and Measurements, para.2, line8-9. "All questionnaires were completed by subjects independently in an adequate space with a firm writing surface and a pencil." Also we added the information of participation and refused participation in Result/Characteristics of Subjects para.1, line1-4.

Methods/Measurement of COPD patients' disease knowledge level, para. 1: This description of the Bristol COPD Knowledge Questionnaire is somewhat confusing and would benefit from some additional information and clarification. Reference is made to “13-item subscales,” but it is presumed that this should be “13 subscales.” What direction is the scoring (high score = high knowledge)?

Given that this measure is not widely known, some description of the types of information assessed in the subscales would be very helpful. There is no information about the measure’s reliability and validity, especially in Chinese. Lastly, because it sounds as though the authors had the measure translated into Chinese, some additional information about the translation methodology would be reassuring.

Answer: Thanks for the comment. As suggested, “13-item subscales” had been changed to “13 subscales”. To make it easy to understand, we added the clarification about the scoring standard that is “The higher score suggested higher disease knowledge level in COPD patients” in Methods/Measurement of COPD patients' disease knowledge level, line 9-10. Also, we made BCKQ information more clear in Methods/Measurement of COPD patients' disease knowledge level. The reliability and validity of both of original edition and translated version had been tested in reference 15, 24.

Methods/Participants and Measurements: There was no description of the CAT Assessment Test.

Answer: Thanks for the comment. CAT is an assessment tool recommended by 2011 GOLD document. In this study, BCKQ and HAD were the major research tools, so we provided detailed description of them. To avoid confusion, there was no description of CAT in this paper.

Statistical analyses: This paragraph would benefit from additional detail and clarity. It is often not clear what variables are being referred to; all variables should be explicitly described. It is also not clear what is meant in the second sentence by “in different group.” The rationale for using partial correlations is not clearly described, and what variable’s effect is being controlled for is not clear. More details are required about the logistic regression in order to fully understand how variables were selected for inclusion and what variables were included in the model.

Answer: Thanks for the comment. As suggested, all variables were added and
explicitly described in Statistical analyses, line2,3. “in different group” means with or without anxiety/depression, and we added the clarification in statistical analyses line4,5. Because partial correlations analysis performed to assessment the correlation between HAD total score and the certain characteristic with the effect of the other characteristics removed, so there had kinds of cases. We have added an additional file for clarifying it [see additional file 1].

About the logistic regression, those variables were put into the analysis, that were significantly related to the HAD total score in spearman correlation analysis. Details of these variables had been description in the Result, section 3 "Determinants of Anxiety and/or Depression in Subjects".

12. Results/Characteristics of Subjects: If the cutoff of 8 on the HADS was used to identify those with anxiety and/or depression, this should be indicated in the Results section (and all tables).

Answer: Thanks for the comment. We have described “a score of 8 or higher on either subscale should be taken as an indication of possible pathology” in Methods/Measurement of anxiety and depression, line 6-7. The similar description “Definition of Anxiety and/or Depression Status: HAS-A #8 and/or HAD-D score #8” in the note of table1 and table3.

13. Results/correlation of HAD Total Score with Characteristics of Subjects, para. 1: The statistics and significance values should be presented in the Results section along with the direction (e.g., is higher HADS score related to being female or male?). It is not clear what the last sentence means. Not all sociodemographic variables were reported; was that intentional?

Answer: Thanks for the comment. In this section, we just shown the variables which revealed significant correlation with HAD total score, and the more details of these results were shown in table 2. The results of spearman correlation analysis were used to find out the variables which should be put into the logistic regression. To avoid confusion, the results were description briefly in that section (Results/correlation of HAD Total Score with Characteristics of Subjects, para.1). Since all details of results were present in the table 2, the last sentence was deleted with less confusion.

14. Results/determinants of Anxiety and/or Depression in Subjects: It is probable that the authors intended to refer to a multivariable model rather than a multivariate model; please clarify.

Answer: Thanks for the comment. The correct interpretation should be “a multivariable model”, and we have revised this words throughout the paper.

15. Discussion, para. 2: The authors seemed to preferentially focus on the results that confirmed the premise of the paper – that patient education about their COPD is related to anxiety and depression levels. However, the model that included the BCKQ was described by the authors as having “weak” predictive capability. In fact, other variables were included in that model and their potential relationship with anxiety and depression were not discussed.

Answer: Thanks for the comment. It is true that the model that included the BCKQ was just having “weak” predictive capability. It's important to note that the
model was used for confirming our hypotheses in another way in this study, although 4 variables (BCKQ, CAT, mMRC and gender) had been identified in partial correlation analysis. Also, the results showed in BCKQ contained some new information that were not present in CAT, mMRC, gender and other characters.

The "weak" revealed the complexity of the relationship between COPD clinical characters and anxiety/depression. Some other studies showed similar results of “weak” predictive capability models, which were based on other characters except COPD knowledge level.

In this paper, our aim was revealed the relationship between COPD patients' disease knowledge level and anxiety/depression. We didn’t discuss CAT, mMRC and gender, because they had been researched and discussed in other studies, for example ECLIPSE (reference 10), including quality of life, symptom and lung function etc.

16. Discussion, para. 3: Considerable emphasis was placed on the significance of specific subdomains of the BCKQ. This paragraph contains considerable conjecture that is not supported by data.

Answer: Thanks for the comment. The conjecture was the reasonable extensions of discussion based on our exploratory research, it was benefit for further research and provided some possible viewpoints.

17. Discussion, para. 4: The limitations section would benefit from some additional consideration by the authors. The sample included a very small number of women (<10%), which was not discussed; the sample also had a largely low education level, so there is reason to believe literacy levels may have been limited. Without information on how the participants completed the measures, readers are unable to determine how much of a factor this may have played in the results, especially given that the manuscript highlights the role of disease-specific education.

Answer: Thanks for the comment. It is true that there was a very small number of women (<10%), due to the gender characteristic of COPD (male ratio is higher than female in the epidemiological investigation, more than 3:1) and the actual ratio of gender in the clinic. The ratio was similar with the other research on COPD. So we had no more to explain it. The sample indeed had a largely low education level also. This is a noteworthy characteristic of COPD patients due to low income and poor living conditions, however, there was no significant correlation between education level with disease knowledge level from the correlations analysis. “how the participants completed the measures” have been added in Methods/Participants and Measurements, para.2, line7-8.

Minor Essential Revisions
1. Title: “studies” should be “study”
Answer: Thanks for the comment. We have revised it.
2. Throughout the manuscript, “wildly” should be “widely”
Answer: Thanks for the comment. We have revised it throughout the manuscript.
3. Throughout the manuscript, there was reference to a score “increase”; since this was a cross-sectional study, scores would not have changed, so it is presumed that this was intended to refer to “higher scores,” but this should be confirmed and then clarified throughout.

Answer: Thanks for the comment. As suggested, we have changed “increase of HAD total score” to “higher HAD total score” for the more appropriate expression throughout the paper.

Reviewer 2:

Minor Essential revisions are required.

1. In the text the word ‘wildly’ needs replacing with ‘widely’.
Answer: Thank you for the comment. The same as above, we have revised it throughout the manuscript.

2. In the conclusions section of the abstract (last sentence) I would change the word intervened to targeted.
Answer: As suggested, we have changed “Intervened” to “targeted” in the abstract.

3. Page two second paragraph delete ‘Determinant factors to Factors that determine...
Answer: As suggested, we have revised it.

4. Page 2 the authors need to change the term ' factors cannot be intervened' ? change this to addressed or reword the sentence.
Answer: As suggested, we have changed “intervened” to “addressed” in page 2.

5. In the last paragraph on background section I would ask the authors to add what disease knowledge consists of. It is explained further in the article but I think it's helpful to clarify here.
Answer: As suggested, in Background, we have added “the COPD knowledge in 13 topics ( including (1) Epidemiology, (2) Aetiology, (3) Symptom, (4) Breathlessness, (5) Phlegm, (6) Infections, (7) Exercise, (8) Smoking, (9) Vaccination, (10) Inhaled bronchodilators, (11) Antibiotics, (12) Oral steroids and (13) Inhaled steroids )” in the last para.

6. In section Participants and Measurements I would change the sentence beginning subjects general medical information. After smoking history I would change the text to highest educational qualification and either delete 'so on' or expand what this is.
Answer: As suggested, we have revised it.

7. Could the authors expand on what they mean about higher education.
Answer: Thank you for the comment. We have expanded what they mean about higher education of “got qualification of junior college or above”.

8. In the first paragraph of the discussion section I would change the last bit of the sentence from less 6MWD to lower 6MWD.
Answer: As suggested, we have changed the sentence from less 6MWD to lower 6MWD.

9. In discussion section do not start a sentence with 'AND.... I would also change the word intervened at the end of that sentence.
Answer: As suggested, we have deleted the start word “And…”, also changed the word “intervened” with “addressed” at the end of that sentence in Discussion para 2.

10. Throughout the document this word 'intervened ' is mentioned. I don’t think this reads well & would recomnned changing to 'addressed or targeted.
Answer: As suggested. We have changed “Intervened” to “addressed” or “targeted” for the more appropriate expression throughout the paper.

11. Reword the next sentences starting with 'But' - Do not start a sentence with But.
Answer: As suggested. We have changed the next sentences starting with 'However' or “while”, not “But”.

12. The discussion sections needs recording as the english is not good.
As suggested, we ask for the advice of a native speaker and carefully revise grammatical errors, and rewrite the unclear terms.
Thank for the reviewer’s helpful comments. We have addressed all the suggestions of the two reviewers. Undoubtedly, the incorporation of these reviewers’ comments has improved the quality and clarity of this manuscript. We believe that these studies present new findings that would be of interest to BMC Pulmonary Medicine readers. We thank again you for your consideration of this manuscript.

Sincerely Yours,
Qianli Ma
Institute of Respiratory Diseases,
Xinqiao Hospital,
Third Military Medical University,
Chongqing 400037, China