

## PEER REVIEW HISTORY

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### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Life Event Stress and Chronic Obstructive Pulmonary Disease (COPD): Associations with Mental Wellbeing and Quality of Life in a Population-based Study
<b>AUTHORS</b>	Ng, Tze Pin ; Lu, Yanxia; Nyunt, Ma Shwe; Gwee, Xinyi; Feng, Liang; Feng, Lei; Kua, Ee Heok; Kumar, Rajeev

### VERSION 1 - REVIEW

<b>REVIEWER</b>	Dr Peter Coventry Research Fellow University of Manchester United Kingdom  No competing interests to declare.
<b>REVIEW RETURNED</b>	12-Jul-2012

<b>THE STUDY</b>	<p>The introduction and methods miss opportunities to state the main research question clearly. I am not sure if the question relates to the hypothesis that people with COPD have poorer coping skills, less resilience and/or fewer social and economic resources to cope with life events and that this leads to higher depression and poorer QOL than people without COPD. Or, are the authors asking whether COPD patients perceive and appraise life events differently to people without COPD and that this different appraisal style is associated with poorer QOL and higher depression?</p> <p>Related to this point is the fact that in the methods it is not clear what the independent variables are and what the dependant variable is. And is there a primary outcome - depression or QOL or cognitive functioning? If the authors were interested in looking at how coping and resilience differed in these populations why did they not measure these psychological attributes? This is something that could be addressed in the limitations section. As could be the problems of using inventories of stressful life events that suffer from inter-categorical variability and recall bias. See Bruce P. Dohrenwend. Psychol Bull. 2006 May ; 132(3): 477-495.</p> <p>The manuscript can be improved editorially. Some of the sentences are not clear and the language at times is not sufficiently scientific. I'm not sure what the authors mean by 'life events aggravate worse mental health and functioning'. Do the authors mean life events were significantly associated with poorer QOL and worse depression in people with COPD compared with people without COPD. Be consistent when reporting the main effects and interaction effects.</p> <p>The introduction lacks some important contextual findings about the prevalence of psychological disorders in COPD e.g. Zhang MWB, Ho RCM, Cheung MWL, Fu E, Mak A. Prevalence of</p>
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	<p>depressive symptoms in patients with chronic obstructive pulmonary disease: a systematic review, meta-analysis and meta-regression. Gen Hosp Psychiatry 2011;33:217-23.</p> <p>Eisner MD, Blanc PD, Yelin EH, Katz PP, Sanchez G, Iribarren C, et al. Influence of anxiety on health outcomes in COPD. Thorax 2010;65:229-34.</p>
<b>RESULTS &amp; CONCLUSIONS</b>	<p>I'm not sure what the research question was so I cannot make an informed judgement about whether the results answer this question.</p> <p>But the findings about the main and interaction effects are plausible and credible. They are however not discussed in a focused way, partly because the main aim of the study appears at the start to be too diffuse. I'm not sure what relevance the discussion of macro-social approaches to the aetiology of COPD has for this paper. The idea that life events may impact on people in different ways and lead to the development of COPD is an interesting one but not relevant - this paper is not about the onset of COPD.</p> <p>The authors also discuss how individuals' internal coping ability and resources will affect how they appraise and perceive life events. And they showed that the perception of stress was the same in COPD and non-COPD individuals, concluding that coping ability does not explain greater psychological morbidity in COPD. But the authors did not measure resilience or coping style. It's a big leap to say that psychobiological (which is a vague term anyway) might therefore explain why COPD patients are more vulnerable to the impact of stress.</p> <p>There is also no applied message. Apart from a single sentence at the end that further studies should look at the role of psychological interventions. To what end. To treat depression and other psychological disorders in COPD patients, because we know these disorders impact on important patient centred outcomes. Or is it about managing psychological ill health better so COPD patients are better able to cope with life events? Or is it about informing clinicians (in primary or specialist settings?) about the occurrence of life events in case it triggers exacerbation of COPD?</p> <p>The statistics in the written results section should include F values and degrees of freedom, as should Table 2. It is also not possible to tell from the figures which line relates to which population group.</p>
<b>GENERAL COMMENTS</b>	<p>This is an interesting piece of work that might add to our understanding about the impact of psychosocial health on important outcomes in COPD patients. However the question is not clear and the discussion too unfocused. The manuscript would also benefit from a more applied focus with key messages for primary care and/or respiratory physicians. As it stands it falls between a paper about an interesting and plausible psychological hypothesis and a plea for more work to prospectively model relationships between life events and physical and mental health in COPD.</p>

<b>REVIEWER</b>	<p>Dr Abebaw Yohannes Reader in Physiotherapy Manchester Metropolitan University</p> <p>I have no competing interests.</p>
<b>REVIEW RETURNED</b>	25-Jul-2012

<b>THE STUDY</b>	<ol style="list-style-type: none"> <li>1. There is no clear justification for the inclusion and exclusion criteria in this population study.</li> <li>2. There is not clear justification for the post-bronchodilator for non-COPD subjects.</li> <li>3. The abstracts lacks clarity in readability this needs tightening up.</li> <li>4. I believe more detail information are required to explain the steps have taken prior to a two way analysis.</li> </ol>
<b>RESULTS &amp; CONCLUSIONS</b>	<ol style="list-style-type: none"> <li>1. Table does not tell whether there are statistical significant difference between the two groups or not.</li> <li>2. It will benefit with the detail discussion focusing on the main findings of the study.</li> </ol>
<b>REPORTING &amp; ETHICS</b>	<ol style="list-style-type: none"> <li>1. COSORT is not applicable in this study.</li> </ol>
<b>GENERAL COMMENTS</b>	<p>General comments and observation  This is interesting study and very little data available that investigated the impact of life event stress in elderly patients with chronic obstructive pulmonary disease (COPD). Findings indicate that life stress events have detrimental effect on the physical functioning and psychological well-being of older patients with COPD in comparison to patients without COPD. Psychosocial factors play an important role in the success of any kind of intervention. Having said that the paper may benefit with more detail comment on the clinical application of the findings in relation to: 1) the cross-sectional nature of the findings whether the effects of life events lead to depression or vice versa 2) the relative small sample size, and 3) lack of longitudinal data.</p> <p>Specific comments</p> <ol style="list-style-type: none"> <li>1. The literature review may benefit with clear, concise and focused appraisal of life events specific to COPD patients. It is quite long-winded and lacks clarity.</li> <li>2. What percentage of the population who were approached either declined or excluded to participate in the study?</li> <li>3. What was the cut off score employed in this study to ensure the participants are cognitively intact using the MMSE?</li> <li>4. The SF-3g was used in this study. However, the authors reported findings only from the component summary of MCS and PCS. What happen to the rest of the SF-3d data?</li> <li>5. In the data analysis section, it will be helpful to state in how the collinearity was tested between the GDS depression and MCS. Both of them are focusing on psychological well-being of the patient.</li> <li>6. It would be helpful to provide further explanation or further steps taken, in how the data analysis was carried –out prior to the two-way analysis. It is worthy of getting some advice (comment) from a statistician.</li> <li>7. Table 1 are there differences between the variables tested between COPD and non-COPD patients.</li> <li>8. What was the reason the non-COPD patients had post-bronchodilator FEV1?</li> <li>9. Table 2 – IADL referring to which variables in the text.</li> <li>10. How many of the participants had GDS&gt; 5 for both patients with and without COPD? It is advisable to comment as well the reliability and validity of the GDS in general population.</li> <li>11. The findings will benefit with more detail discussion of the “ ... life event stress was associated with more depressive symptoms and worse mental and physical functioning in both COPD and non-COPD participants (main effects) but this effect was much more aggravated in COPD than in non-COPD individuals (interactive effect). What does this mean to clinicians who are working in the field?</li> </ol>

## VERSION 1 – AUTHOR RESPONSE

Reviewer 1:

1) The introduction and methods miss opportunities to state the main research question clearly. I am not sure if the question relates to the hypothesis that people with COPD have poorer coping skills, less resilience and/or fewer social and economic resources to cope with life events and that this leads to higher depression and poorer QOL than people without COPD. Or, are the authors asking whether COPD patients perceive and appraise life events differently to people without COPD and that this different appraisal style is associated with poorer QOL and higher depression?

The main research question we investigated in this study was whether life event stress was associated with more depressive symptoms and poorer QOL among COPD individuals than among non-COPD individuals. Hypothetically, the association may be explained by the possibility that COPD individuals have poorer coping skills, less resilience and/or fewer social and economic resources, or COPD individuals perceive and appraise life events differently to people without COPD, or both. While we raised these possible explanations in the Introduction, these hypotheses were not directly tested in this study. To make the main research question clear in the Introduction, we have moved these statements to the Discussion, where we discussed these hypothetical explanations and provided indirect evidence to suggest that perception and appraisal of life event did not appear to be responsible for more depressive symptoms and poorer QOL among COPD individuals. In the Introduction, we now state our main research question explicitly “.....whether common life event stress is associated with greater psychological distress and poorer quality of life in older individuals with COPD, in comparison to their counterparts without COPD.”

Related to this point is the fact that in the methods it is not clear what the independent variables are and what the dependent variable is. And is there a primary outcome - depression or QOL or cognitive functioning? If the authors were interested in looking at how coping and resilience differed in these populations why did they not measure these psychological attributes? This is something that could be addressed in the limitations section. As could be the problems of using inventories of stressful life events that suffer from inter-categorical variability and recall bias. See Bruce P. Dohrenwend. *Psychol Bull.* 2006 May ; 132(3): 477–495.

The independent and dependent variables are now clearly stated in the revisions to the last paragraph in the Introduction and the Method. We make it clear that the independent variable of primary interest was life event stress, and the primary outcome variables of interest were depressive symptoms and quality of life. COPD status was also an independent variable, but the main effects of COPD on pulmonary and cognitive function were of secondary interest, and represent incidental findings. These points were reiterated in the Discussion.

The study aimed to investigate “whether common life event stress was associated with greater psychological distress and poorer quality of life in older individuals with COPD, in comparison to their counterparts without COPD.” It did not aim to look at how coping and resilience differed in participants with or without COPD. We did not measure coping resources or appraisal style. There was an unfortunately redundant content related to coping or resilience in the introduction. We have deleted this in the revised paper. In the discussion section, we added that “A greater detrimental effect of life event stress on psychological wellbeing and quality of life in COPD individuals may hypothetically be explained by the possibility that COPD individuals perceive and appraise stressful life events differently to individuals without COPD, or that COPD individuals have poorer coping skills or fewer social and economic resources, or both. We did not have measures of cognitive appraisal, coping resources and social support to explore these hypotheses directly, and this is a limitation of our study.”

In the Discussion section, we have added that “Furthermore, the use of life event inventories to appraise the stressfulness of life event has limitations including inter-categorical variability and recall bias [34].

2) The manuscript can be improved editorially. Some of the sentences are not clear and the language at times is not sufficiently scientific. I'm not sure what the authors mean by 'life events aggravate worse mental health and functioning'. Do the authors mean life events were significantly associated with poorer QOL and worse depression in people with COPD compared with people without COPD. Be consistent when reporting the main effects and interaction effects.

We have edited the manuscript substantially for clearer scientific reporting. We have re-stated our findings in the following places:

Abstract: “...life event stress was associated with more depressive symptoms and worse quality of life in individuals with COPD, much more than in those without COPD.”

Discussion section: “...that life event stress was associated with depressive symptoms and poor quality of life in both COPD and non-COPD participants (main effects), but showed a significantly stronger association among individuals with COPD than among non-COPD individuals (interaction), suggesting a disproportionately greater detrimental effect.”

Conclusion: “life event stress was associated with more depressive symptoms and worse quality of life in individuals with COPD, much more than in those without COPD.”

3) The introduction lacks some important contextual findings about the prevalence of psychological disorders in COPD. e.g.

Zhang MWB, Ho RCM, Cheung MWL, Fu E, Mak A. Prevalence of depressive symptoms in patients with chronic obstructive pulmonary disease: a systematic review, meta-analysis and meta-regression. *Gen Hosp Psychiatry* 2011;33:217-23.

Eisner MD, Blanc PD, Yelin EH, Katz PP, Sanchez G, Iribarren C, et al. Influence of anxiety on health outcomes in COPD. *Thorax* 2010;65:229-34.

We have noted these important contextual findings about the prevalence of psychological disorders in COPD and added these two references at the first paragraph of the manuscript.

4) I'm not sure what the research question was so I cannot make an informed judgement about whether the results answer this question. But the findings about the main and interaction effects are plausible and credible. They are however not discussed in a focused way, partly because the main aim of the study appears at the start to be too diffuse. I'm not sure what relevance the discussion of macro-social approaches to the aetiology of COPD has for this paper. The idea that life events may impact on people in different ways and lead to the development of COPD is an interesting one but not relevant - this paper is not about the onset of COPD.

We have now made our hypothesis clearer and our discussion more focused on our own results in answering our research question “... whether life event stress is associated with greater psychological distress and poorer quality of life in older individuals with COPD, in comparison to their counterparts without COPD

We agree that the discussion of macro-social factors in the aetiology of COPD (the idea that life events may impact on people in different ways and lead to the development of COPD) has no relevance for this paper, as the paper is not about the onset of COPD. This has been deleted in the revised manuscript.

The authors also discuss how individuals' internal coping ability and resources will affect how they appraise and perceive life events. And they showed that the perception of stress was the same in COPD and non-COPD individuals, concluding that coping ability does not explain greater psychological morbidity in COPD. But the authors did not measure resilience or coping style. It's a big leap to say that psychobiological (which is a vague term anyway) might therefore explain why COPD patients are more vulnerable to the impact of stress.

We agree that in showing that the perception of stress was the same in COPD and non-COPD individuals, we could not conclude that coping ability explained the greater psychological morbidity in COPD in our study, because we did not measure cognitive appraisal or coping resources.

We have instead commented that "A greater detrimental effect of life event stress on psychological wellbeing and quality of life in COPD individuals may hypothetically be explained by the possibility that COPD individuals perceive and appraise stressful life events differently to individuals without COPD, or that COPD individuals have poorer coping skills or fewer social and economic resources, or both. We did not have measures of cognitive appraisal, coping resources and social support to explore these hypotheses directly, and this is a limitation of our study.

In the revised manuscript, we have gone further to refer to the few available studies that have investigated the relationship between cognitive appraisal of stressful events, coping strategies and psychological distress in COPD patients. This included a study by Andrenas and co-investigators [23] which found that neither types of stressful event, stress intensity, primary or secondary appraisal, or number of coping strategies used were significantly related to psychological distress. Only problem-solving coping strategies were inversely related to psychological distress. This suggests that poor coping skills may be a principal psychological problem among COPD patients that contribute to their psychological distress and poor quality of life. However, further studies should be conducted."

We have omitted the statement that an underlying psychobiological basis may explain why COPD patients are more vulnerable to the adverse health and functional impacts of stress.

There is also no applied message. Apart from a single sentence at the end that further studies should look at the role of psychological interventions. To what end. To treat depression and other psychological disorders in COPD patients, because we know these disorders impact on important patient centred outcomes. Or is it about managing psychological illness better so COPD patients are better able to cope with life events? Or is it about informing clinicians (in primary or specialist settings?) about the occurrence of life events in case it triggers exacerbation of COPD?

We added one paragraph for our applied message "Studies [35-37] have reported that mental health status, such as anxiety and depressive symptoms, are better predictors of COPD-related quality of life than pulmonary function. The present study supports this observation and further indicates that life event stress has a starkly detrimental effect on mental health and quality of life in patients with COPD. While it is increasingly being recognized that the identification and treatment of psychological disorders are important for improving patient centered outcomes in COPD patients, there should be commensurate attention to the identification of stressful life event(s) that trigger psychological disturbances and poor psycho-social functioning. Psychological interventions in COPD patients that include the identification of stressful life event and improving patients' coping skills may directly contribute to improving psychological functioning and quality of life in COPD patients.

5) The statistics in the written results section should include F values and degrees of freedom, as should Table 2. It is also not possible to tell from the figures which line relates to which population group.

We have added F values and degrees of freedom in the written results section and degrees of freedom in Table 2. We had legend at the right side of the figure that the blue line is for non-COPD and the green line represents the COPD group.

Reviewer 2:

1) There is no clear justification for the inclusion and exclusion criteria in this population study. We have explained inclusion and exclusion criteria in the method section “We interviewed one participant from each household who were Singaporean citizens or permanent residents aged 65 or older who were able to give informed consent. Those who were too frail or ill and unable to complete the interview, for reasons such as from post-stroke aphasia, cachexia or profound dementia, were excluded.

2) There is not clear justification for the post-bronchodilator for non-COPD subjects. Post-bronchodilator spirometry represents the standard procedure to diagnose COPD in population surveys of COPD prevalence. Post-bronchodilator FEV1/FVC < 0.70 is the standard criteria to define participants with or without COPD.

3) Revision of abstract.

We have revised the Abstract as follows:

Introduction: “The aim of this study was to investigate whether life event stress was associated with greater psychological distress and poorer quality of life in older individuals with COPD, in comparison to their counterparts without COPD.”

Conclusion: “Our findings indicate that life event stress was associated with more depressive symptoms and worse quality of life in individuals with COPD, much more than in those without COPD. Further studies should explore the role of cognitive appraisal of stress, coping resources and psychosocial support in this relationship.”

4) I believe more detail information are required to explain the steps have taken prior to a two way analysis.

The preliminary analysis prior to two-way ANOVA is explained in more details in the Method. “In preliminary univariate analysis, participants with and without COPD were compared with respect to differences in number of life events, and perceived stress score, level of FEV1, CFQ, MMSE, GDS depression, SF-36 PCS and SF-36 MCS scores, as well as potential confounding variables, sex, age, ethnicity, smoking status, number of chronic diseases, using t-tests or chi-squared tests of significance. The independent main effects of life event stress and COPD (independent variables) as well as the interaction effects of life event stress and COPD on measures of pulmonary function, depressive symptoms, cognitive function, and quality of life (dependent variables) were analyzed using two-way analysis of variance (ANOVA) and general linear model which adjusted for sex, age, ethnicity, smoking status, and number of chronic illness. The independent variable of primary interest was life event stress, and the primary outcome variables of interest were depressive symptoms and quality of life. A secondary relationship analyzed in the two-way ANOVA model was the main effect of COPD status (and its interaction with life event stress) on primary outcomes of pulmonary and cognitive function.

This is further elaborated in the Results on page 7 and 8.

5) Table does not tell whether there are statistical significant differences between the two groups or

not.

Table 1: t test and  $\chi^2$  values and p values have been added to the unadjusted mean and SD values of variables for participants with and without COPD.

6) It will benefit with the detail discussion focusing on the main findings of the study.

The Discussion is revised to focus on the main findings of the study. The unrelated comments on the macro-social factors associated with the development of COPD have been deleted. An additional paragraph on the practical implications of the findings is included.

#### General comments and observation

1) This is interesting study and very little data available that investigated the impact of life event stress in elderly patients with chronic obstructive pulmonary disease (COPD). Findings indicate that life stress events have detrimental effect on the physical functioning and psychological well-being of older patients with COPD in comparison to patients without COPD. Psychosocial factors play an important role in the success of any kind of intervention. Having said that the paper may benefit with more detail comment on the clinical application of the findings in relation to: 1) the cross-sectional nature of the findings whether the effects of life events lead to depression or vice versa 2) the relative small sample size, and 3) lack of longitudinal data.

We have commented that "In a cross-sectional study, interpreting the causal relationship between stress and the health-related functional outcomes can be uncertain. Further longitudinal studies are required."

#### Specific comments

1) The literature review may benefit with clear, concise and focused appraisal of life events specific to COPD patients. It is quite long-winded and lacks clarity.

The literature review has been rewritten to focus on the life events stress in relation to COPD health and quality of life outcomes. Paragraphs 2 and 3 have largely been removed and replaced with a more concise review and arguments leading to the aims of the study.

2) What percentage of the population who were approached either declined or excluded to participate in the study?

In the revised paper, we have added that the participants who completed interviews and provided technically acceptable spirometric data (N=497) represented a response rate of 78.5% of the eligible participants

3) What was the cut off score employed in this study to ensure the participants are cognitively intact using the MMSE?

The cutoff score of MMSE to determine cognitive impairment is 23 or less.

4) The SF-36 was used in this study. However, the authors reported findings only from the component summary of MCS and PCS. What happen to the rest of the SF-36 data?

Data from all 36 items in the SF-36 are used to compute scores for eight domain subscales or two weighted summary measures of physical and mental health function: Physical Health Component Score and the Mental Health Component Score, which are widely used in many studies and in this study. References:

Ware JE, Kosinski M, Keller SD. SF-36 Physical and Mental Health Summary Scales: A

users manual. The Health Institute, New England Medical Centre, Boston, Massachusetts, December 1994. 4th printing.

Aguilar-Navarro S, Navarrete-Reyes AP, Grados-Chavarría BH, García-Lara JM, Amieva H, Avila-Funes JA. The Severity of Urinary Incontinence Decreases Health-Related Quality of Life among Community-Dwelling Elderly. *J Gerontol A Biol Sci Med Sci*. 2012 Aug 9.

Akinci AC, Pinar R, Demir T. The relation of the subjective dyspnoea perception with objective dyspnoea indicators, quality of life and functional capacity in patients with COPD. *J Clin Nurs*. 2012 Jul 5. doi: 10.1111/j.1365-2702.2012.04161.x.

5) In the data analysis section, it will be helpful to state in how the collinearity was tested between the GDS depression and MCS. Both of them are focusing on psychological well-being of the patient.

Both GDS depression and MCS are indeed related measures of psychological well-being. However, in our study they are analyzed separately as dependent variables in different regression models, and not as independent variables, hence did not pose problems of collinearity in regression models.

6) It would be helpful to provide further explanation or further steps taken, in how the data analysis was carried out prior to the two-way analysis. It is worthy of getting some advice (comment) from a statistician.

We have responded to this above and explained in the Method and Results sections that:

“In preliminary univariate analysis, participants with and without COPD were compared with respect to differences in number of life events, and perceived stress score, level of FEV1, CFQ, MMSE, GDS depression, SF-36 PCS and SF-36 MCS scores, as well as potential confounding variables, sex, age, ethnicity, smoking status, number of chronic diseases, using t-tests or chi-squared tests of significance. The independent main effects of life event stress and COPD (independent variables) as well as the interaction effects of life event stress and COPD on measures of pulmonary function, depressive symptoms, cognitive function, and quality of life (dependent variables) were analyzed using two-way analysis of variance (ANOVA) and general linear model which adjusted for sex, age, ethnicity, smoking status, and number of chronic illness. The independent variable of primary interest was life event stress, and the primary outcome variables of interest were depressive symptoms and quality of life. A secondary relationship analyzed in the two-way ANOVA model was the main effect of COPD status (and its interaction with life event stress) on primary outcomes of pulmonary and cognitive function.

This is further elaborated in the Results on page 7 and 8.

7) Table 1 are there differences between the variables tested between COPD and non-COPD patients.

Table 1: t test and  $\chi^2$  values and p values have been added to the unadjusted mean and SD values of variables for participants with and without COPD.

8) What was the reason the non-COPD patients had post-bronchodilator FEV1?

Post-bronchodilator spirometry is the standard procedure to diagnose COPD in population surveys of COPD prevalence. Post-bronchodilator FEV1/FVC < 0.70 is the standard criteria to define participants with or without COPD.

9) Table 2 – IADL referring to which variables in the text.

Apology: IADL was not a variable in our analysis. We have deleted IADL in the notes of Table 2.

10) How many of the participants had GDS > 5 for both patients with and without COPD? It is advisable to comment as well the reliability and validity of the GDS in general population.

We have added in Table 1, % (n) of GDS ≥ 5 in participants with and without COPD. We have included the following additional information in the Method: “In validation studies in the local older population [17], translated versions of the GDS-15 have been found to be a valid and reliable screening tool for depression: Cronbach’s alpha of 0.80, and intraclass coefficients of test-retest reliability of 0.83 and inter-rater reliability of 0.94. Using a GDS cutoff of ≥ 5, the GDS-15 has a sensitivity of 0.97 and specificity of 0.95 (area under curve of 0.98) for determining major depressive disorder according to DSM-IV criteria. Depressive symptoms defined as such by GDS ≥ 5 is clinically significant, and such cases including “sub-threshold” depression, had been shown in the same population to be associated with significantly poorer mental and physical health and functional status, and more healthcare resource utilization compared to non-cases and were similar to or worse than syndrome threshold cases of depression [18].

References:

17. Nyunt, M.S.Z., Fones, C., Niti, M. and Ng, T.P. (2009). Criterion-based validity and reliability of the Geriatric Depression Screening Scale (GDS-15) in a large validation sample of community-living Asian older adults. *Aging & Mental Health*, 13(3), 376–382.
18. Soh, K.C., Kumar, R., Niti, M., Kua, E.H. and Ng, T.P. (2008). Subsyndromal depression in old age: clinical significance and impact. *International Psychogeriatrics*, 20(1), 188-200.

11) The findings will benefit with more detail discussion of the “ ... life event stress was associated with more depressive symptoms and worse mental and physical functioning in both COPD and non-COPD participants (main effects) but this effect was much more aggravated in COPD than in non-COPD individuals (interactive effect). What does this mean to clinicians who are working in the field?

We added this paragraph commenting on the clinical implications of these findings. “Studies [31-33] have reported that mental health status, including anxiety and depressive symptoms, are better predictors of COPD-related quality of life than pulmonary function. The present study supports this observation and further indicates that life event stress has a starkly detrimental effect on mental health and quality of life in patients with COPD. While it is increasingly being recognized that the identification and treatment of psychological disorders are important for improving patient centered outcomes in COPD patients, there should be commensurate attention to stressful life event(s) that trigger psychological disturbances and poor psycho-social functioning. Psychological interventions in COPD patients that include the identification of stressful life event and improving patients’ coping skills may directly contribute to improving psychological functioning and quality of life in COPD patients.”

#### VERSION 2 – REVIEW

<b>REVIEWER</b>	Peter Coventry Insitute of Population Health University of Manchester England, UK  No competing interests
<b>REVIEW RETURNED</b>	08-Oct-2012

<b>GENERAL COMMENTS</b>	The authors have made every effort to address the main queries raised in the initial peer review. The main improvement is that the research question is much clearly articulated and the results relate
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	<p>more faithfully to these questions. The authors should add a note about what the statistics package is as it is not familiar to me and add any reference for this.</p> <p>I'm still not entirely convinced that the authors' discussion completely addresses all relevant issues and the implications for research and practice section is still a little weak. For example, they allude to work to develop psychological interventions to improve coping skills but it is not clear if such interventions are the same as the ones used to improve mood and reduce anxiety or if there is need to develop more innovative ways to support COPD patients during life stress to prevent the onset of mood and anxiety disorders. This has policy implications as for example, in the UK, NICE recommend psychological interventions to treat mild to moderate depression in COPD but this approach is not indicated for supporting people experiencing stressful life events. Nor is it clear if this is something for primary or secondary care to focus on. Perhaps the authors may want to earmark a separate section of the manuscript that specifically looks at implications for practice and research.</p>
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## VERSION 2 – AUTHOR RESPONSE

### Revision and Response to Comments

1) The authors should add a note about what the statistics package is as it is not familiar to me and add any reference for this.

The PASW Statistics version 18 is the SPSS Statistics package version 18 that was bought over by Lenovo (IBM). Since then, subsequent SPSS package version 20 has been renamed IBM SPSS version 20. In the revised manuscript we have added 'SPSS' to "PASW Statistics (SPSS) version 18".

2) The implications for research and practice section is still a little weak. For example, they allude to work to develop psychological interventions to improve coping skills but it is not clear if such interventions are the same as the ones used to improve mood and reduce anxiety or if there is need to develop more innovative ways to support COPD patients during life stress to prevent the onset of mood and anxiety disorders. This has policy implications as for example, in the UK, NICE recommend psychological interventions to treat mild to moderate depression in COPD but this approach is not indicated for supporting people experiencing stressful life events. Nor is it clear if this is something for primary or secondary care to focus on. Perhaps the authors may want to earmark a separate section of the manuscript that specifically looks at implications for practice and research.

We have included an additional paragraph in the Discussion as such:

"Studies [33-35] have reported that mental health status, including anxiety and depressive symptoms is a better predictor of COPD-related quality of life than pulmonary function. The present study supports this observation and further indicates that life event stress has a starkly detrimental effect on mental health and quality of life in patients with COPD. More studies of the effects of stress management and coping strategy in psychological interventions in COPD should be investigated in randomized controlled clinical trials.

It is increasingly being recognized that the identification of psychological disorders, and psychological and psychosocial interventions to improve mood and reduce anxiety are important for improving patient centered outcomes in COPD patients. However, in published clinical guidelines such as NICE, where the initial step care management by practitioners in primary care and general hospital settings includes low-intensity psychosocial interventions for patients with persistent subthreshold depressive

symptoms or mild to moderate depression, there appears to be little attention given to identifying stressful life event(s) and supporting COPD patients experiencing stressful life events to prevent the onset of mood and anxiety disorders. In particular, group-based peer support, individual guided self-help based on cognitive behavioural therapy (CBT) principles or computerised CBT to reduce patients' vulnerability to stress may usefully include objective cognitive appraisal of stress, problem-solving coping skills, and relaxation therapy to help support COPD patients experiencing stressful life events."