PEER REVIEW HISTORY

This paper was submitted to a another journal from BMJ but declined for publication following peer review. The authors addressed the reviewers' comments and submitted the revised paper to BMJ Open. The paper was subsequently accepted for publication at BMJ Open.

(This paper received three reviews from its previous journal but only two reviewers agreed to published their review.)

ARTICLE DETAILS

TITLE (PROVISIONAL)	Coping, mood, and health-related quality of life: A cross-sectional study in Chinese patients with advanced lung cancer
AUTHORS	He, Yaping; Jian, Hong; Yan, Meiqiong; Zhu, Jingfen; Li, Guohong; Lou, Vivian W. Q.; Chen, Jieling

VERSION 1 – REVIEW

REVIEWER	Suzanne Chambers Griffith University
REVIEW RETURNED	06-May-2018

GENERAL COMMENTS	The study assessed mood, coping and HRQOL in 264 patients with Stage 3 and 4 lung cancer. Assessment included: Medical Coping Modes Questionnaire, Positive and Negative Affect Schedule, and 5-level EuroQol 5-dimension instrument. Overall the study is well written. Key study limitations are the cross sectional design and convenience sampling. These are acknowledged. The key issue then for a study that is examining within group effects is that there does not appear to be an overarching guiding theoretical framework for the study. So from this, why would you assume that mood mediates the effect of coping on QOL? It is equally plausible that coping efforts would mediate the effect of mood on QOL. Points to address: • A theoretical framework is needed to support the analytic approach • A discussion of how the results relate to cultural attitudes in Chinese populations to cancer is needed. I would like to see this integrated into both the Introduction and the Discussion, and should link to theory.

REVIEWER	Laurie Steffen Postdoctoral Fellow Wake Forest School of Medicine
REVIEW RETURNED	04-Jun-2018

GENERAL COMMENTS	In "Coping and health-related quality of life in patients with advanced lung cancer: the mediating role of positive and negative mood," authors present mediation analyses from a cross-sectional study assessing coping (confrontation, resigned acceptance), mood (positive and negative) and quality of life (domains and utility

	index). Overall, this manuscript offers a number of important strengths, including sample size and assessment of clinical factors. I have a few major concerns and minor concerns for authors to address to improve the contribution to the literature. Major concerns: Introduction: Authors correctly note several studies that have examined coping style or mood in relation to quality of life in lung cancer patients. However, they assert that mood as a pathway between coping and quality of life has not been examined. The Intro would benefit from mention of theoretical models of coping and mood or coping and qol in illness (e.g., Folkman and Greer; note Roberts' 2018 Psychooncology article on a revised model of Folkman and Greer's for advanced cancer). Authors also should provide more attention to the concept of resigned acceptance. For example, resigned acceptance is different from the concept of acceptance in Acceptance and Commitment Therapy, but how authors describe it in the Intro (i.e., "accept without endeavors to alter the stressful situation") is not specific enough to help distinguish it from ACT's concept of acceptance, which has been associated with adaptive functioning/positive outcomes, unlike resigned acceptance. Some of what authors describe in the Discussion on page 25 would be helpful to state in the Introduction. p. 17 "lung cancer type (poorly differentiated vs. small cell)" -- The distinction between small cell and non-small cell makes sense. I'm somewhat worried about using statistical significance to choose to compare small cell vs. poorly differentiated. SC is certainly different clinically from NSC. Of NSC, squamous seems most distinct from other NSCs. If authors want to distinguish like this, I wonder about NSC - squamous, all other NSCs, vs. SC. If authors leave it as is, they should justify their choice and then comment on why we might expect to see effects based on histology differences. Similarly, authors are right to note that financial stress is a significant concern in the cancer survivorship/qol literature. However, authors should provide more background on why this factor is an important covariate and comment more on how to address it in the Discussion given that it emerged as a significant factor in qol in this sample. Discussion: Can authors give examples of interventions that have targeted mood and/or coping or provide more intervention direction? Minor concerns: Method: p. 7 "oncology medicine recommended the eligible patients" -- can authors clarify whether this means that the oncology team was sending pts to the study vs. just giving the okay to approach a pt (i.e., medically appropriate to approach vs. "I think this would be a good patient for the study")? As written, there is some concern about selection bias. p. 8 line 14 -- please given examples of "acceptance-resignation" coping Results:

	p. 10 line 33 -- "more than 90% of the participants received chemotherapy" -- Clarify whether they were currently receiving chemotherapy and other oncologic tx vs. post-treatment p.15 line 7 "Patients reporting no perceived financial burden..." -- As written, it seems that you dichotomized financial distress, but I believe you treated this as a continuous variable?

REVIEWER	Natasja Raijmakers Netherlands Comprehensive Cancer Organization (IKNL)
REVIEW RETURNED	06-Jun-2018

GENERAL COMMENTS	This study addresses the relationships between coping, mood, and HRQoL among patients with advanced lung cancer. The authors examined the effect of confrontation and resigned acceptance coping on positive mood, negative mood, and HRQoL, and tested mediating role of positive and negative mood in the relationship between coping and HRQoL. A consecutive sample from one hospital in China was used and 328 patients were included in the cross-sectional study. These patients completed a face to face interview with medical students including the following outcomes: EQ5D, MCMQ and PANAS. It is a well-conducted study, with interesting results. However, a up-to-date knowledge of the literature on coping, mood and QoL seems missing, what hampers the interpretation of the findings of this study. Major • The manuscript is in need of English revision. I would suggest a professional English writer to correct the manuscript to improve its readability and clarity. • What is the rational to include only patient with an expected survival time of at least 3 months? • Is the main outcome HRQoL best measured by the EQ5D? This measure is not well validated in advanced cancer patients, see review of Roij, J van et al 2018 in Quality of Life Research • I would strongly suggest to divide table 1 into two separate tables, one with only the background variables and one with the outcomes of the measurements. Now it is a huge table with many subgroups. Some subgroups are too small to report anyway. • To add to the previous point: I am wondering if the analysis of variance test as presented on page 15, line 17-34 is contributing to this paper. I would suggest to leave this out, especially as comparing subgroups was not the aim of the study and the subgroups have no real rational why they would differ on HRQoL. For example in different treatment groups it is clear that HRqOl can differ, but is this due to the treatment or due to selection bias? Minor • I would suggest to have a good look at literature, as the authors claim to be the first study to examine the relationship between coping, mood and QoL in advanced lung cancer. This previous study has done the same: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5160928/ • Page 4, line 43 “two coping strategies .. are regarded as important in cancer pt. This reference is from 1987 and therefor outdated. Please update literature on coping strategies in cancer. More than 2 strategies are present • It may help if you would include a flowchart of the inclusion of the patients: XX asked, 328 included with LC, of these 267 had advanced-stage LU and of them 261 had provided complete

	information. Please add the number of patients that were approached for the study in total and the number of patients who refused. This is helpful for interpretation of the generalizability. • In Table 1 Time of diagnosis does not add up to 261. Please indicate the missings with an asterisk • Please add information on how strong the correlation is, when reporting about is, as done on page 15, line 3-14. “Age was inversely….. from slight to severe.”

REVIEWER	Ramses Sadek Augusta University, Georgia Cancer Center US
REVIEW RETURNED	12-Jul-2018

GENERAL COMMENTS	For the Stepwise regression method, Need to clarify is this regular stepwise (variables can enter and leave) of forward variable selection. I see more than one variable entered at a time which is not common. Need to clarify.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Reviewer Name: Suzanne Chambers
Institution and Country: Griffith University
Please state any competing interests or state ‘None declared’: None declared

Please leave your comments for the authors below
The study assessed mood, coping and HRQOL in 264 patients with Stage 3 and 4 lung cancer. Assessment included: Medical Coping Modes Questionnaire, Positive and Negative Affect Schedule, and 5-level EuroQol 5-dimension instrument.
Overall the study is well written. Key study limitations are the cross sectional design and convenience sampling. These are acknowledged.
The key issue then for a study that is examining within group effects is that there does not appear to be an overarching guiding theoretical framework for the study. So from this, why would you assume that mood mediates the effect of coping on QOL? It is equally plausible that coping efforts would mediate the effect of mood on QOL.
Points to address:

- A theoretical framework is needed to support the analytic approach

Authors’ response: Thanks much for your review and suggestions. In the revised manuscript, theoretical background for the mediating role of mood has been discussed and integrated into the introduction and discussion. We believe that treating mood as a mediator is theoretically sound. However, we understand that there is always possibility for a bi-directional relationship, which could be better tested using longitudinal design.

- A discussion of how the results relate to cultural attitudes in Chinese populations to cancer is needed.

I would like to see this integrated into both the Introduction and the Discussion, and should link to theory.

Authors’ response: Appreciate for your thoughts on the cultural attitudes related to cancer in Chinese populations.
We introduce the cultural views of illness in China and integrate them into the discussion of results. It

may help the readers to have a board view on the contextual background of the two studied coping strategies, and facilitate the understanding of the effects of the coping that were identified in the current study.

Reviewer: 2
Reviewer Name: Laurie Steffen
Institution and Country: Postdoctoral Fellow, Wake Forest School of Medicine
Please state any competing interests or state ‘None declared’: None declared

Please leave your comments for the authors below
In "Coping and health-related quality of life in patients with advanced lung cancer: the mediating role of positive and negative mood," authors present mediation analyses from a cross-sectional study assessing coping (confrontation, resigned acceptance), mood (positive and negative) and quality of life (domains and utility index). Overall, this manuscript offers a number of important strengths, including sample size and assessment of clinical factors. I have a few major concerns and minor concerns for authors to address to improve the contribution to the literature.

Major concerns:
Introduction: Authors correctly note several studies that have examined coping style or mood in relation to quality of life in lung cancer patients. However, they assert that mood as a pathway between coping and quality of life has not been examined. The Intro would benefit from mention of theoretical models of coping and mood or coping and qol in illness (e.g., Folkman and Greer; note Roberts' 2018 Psychooncology article on a revised model of Folkman and Greer's for advanced cancer). Authors also should provide more attention to the concept of resigned acceptance. For example, resigned acceptance is different from the concept of acceptance in Acceptance and Commitment Therapy, but how authors describe it in the Intro (i.e., "accept without endeavors to alter the stressful situation") is not specific enough to help distinguish it from ACT's concept of acceptance, which has been associated with adaptive functioning/positive outcomes, unlike resigned acceptance. Some of what authors describe in the Discussion on page 25 would be helpful to state in the Introduction.

Authors’ response: Thanks very much for your comments and suggestions on the literature!
We revised the 6th paragraph in introduction section by adding the illustration on the mediating role of mood from the theoretical models of stress and coping, and the empirical studies.
Resigned acceptance is different from the concept of acceptance in Acceptance and Commitment Therapy, which is active form of acceptance and characterized by active embrace of thoughts and feelings without unnecessary attempts to alter them. We have clarified the concept of resigned acceptance in the 4th paragraph in introduction section.

p. 17 "lung cancer type (poorly differentiated vs. small cell)" -- The distinction between small cell and non-small cell makes sense. I'm somewhat worried about using statistical significance to choose to compare small cell vs. poorly differentiated. SC is certainly different clinically from NSC. Of NSC, squamous seems most distinct from other NSCs. If authors want to distinguish like this, I wonder about NSC - squamous, all other NSCs, vs. SC. If authors leave it as is, they should justify their choice and then comment on why we might expect to see effects based on histology differences.

Authors’ response: Thanks for the careful suggestions on the lung cancer type.
Lung cancer type (see Table 1) is classified into NSC – adenocarcinoma, NSC – squamous, NSC – poorly differentiated (undifferentiated), NSC – others, Small cell. In the following analyses, we grouped them into three groups: NSC-poorly differentiated, other NSCs, and small cell. In the

multivariate regression analyses (see Table 3) or mediation analyses, the other NSCs was treated as reference group. The reason for this grouping considered the clinical classification system (small cell vs. non-small cell) and statistical significance in this sample (other non-small cell vs. non-small cell – poorly differentiated).

Similarly, authors are right to note that financial stress is a significant concern in the cancer survivorship/qol literature. However, authors should provide more background on why this factor is an important covariate and comment more on how to address it in the Discussion given that it emerged as a significant factor in qol in this sample.

Authors' response: Based on our previous study (Chen, Lou, Jian, et al., 2018), subjective financial burden (i.e., self-perceived financial burden), is an important predictor for HRQoL in lung cancer patients. Therefore, we controlled this significant correlate in the multivariate analysis. A background has been added in the introduction with regard to a range of potential correlates, and an explanation has been provided in the discussion.

Chen JE, Lou VW, Jian H et al. Objective and subjective financial burden and its associations with health-related quality of life among lung cancer patients. Supportive Care in Cancer 2018; 26: 1265-1272.

Discussion: Can authors give examples of interventions that have targeted mood and/or coping or provide more intervention direction?

Authors' response: Examples of interventions (e.g., ACT, early palliative care) has been provided in the discussion of implications.

Minor concerns:
Method:
p. 7 "oncology medicine recommended the eligible patients" -- can authors clarify whether this means that the oncology team was sending pts to the study vs. just giving the okay to approach a pt (i.e., medically appropriate to approach vs. "I think this would be a good patient for the study")? As written, there is some concern about selection bias.

Authors' response: The current study used consecutive sampling. Doctors and nurses at the inpatient unit of department of chest-oncology medicine screened the eligible patients based on the inclusion and exclusion criteria, and researcher approached them and introduced the study.

p. 8 line 14 -- please given examples of "acceptance-resignation" coping

Authors' response: Sample items for acceptance-resignation subscale have been added in the measure section.

Results:
p. 10 line 33 -- "more than 90% of the participants received chemotherapy" -- Clarify whether they were currently receiving chemotherapy and other oncologic tx vs. post-treatment

Authors' response: Thanks for the questions. It has been changed into "more than 90% of the participants had ever received chemotherapy". It refers to treatment history, which included treatments that were received recently or previously.

p.15 line 7 "Patients reporting no perceived financial burden..." -- As written, it seems that you dichotomized financial distress, but I believe you treated this as a continuous variable?

Authors' response: Thanks for the clarification. Perceived cancer-related financial burden was assessed by the question, "Have your disease and treatment caused you and your family financial difficulty", and participants answered on a 5-point scale ranging from 0 (No) to 4 (Very much). Financial burden is treated as a continuous variable in the analysis.
However, as suggested by Dr. Raijmakers (Reviewer 3), we leave out the paragraph discussing the socio-demographic and clinical correlates of mood and HRQoL since it's not the aim of study. Nevertheless, we included these significant correlates (age, gender, cancer stage, lung cancer type, financial burden, a history of radiotherapy) in the multivariate analyses and mediation analyses.

Reviewer: 3
Reviewer Name: Natasja Raijmakers
Institution and Country: Netherlands Comprehensive Cancer Organization (IKNL)
Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below
This study addresses the relationships between coping, mood, and HRQoL among patients with advanced lung cancer. The authors examined the effect of confrontation and resigned acceptance coping on positive mood, negative mood, and HRQoL, and tested mediating role of positive and negative mood in the relationship between coping and HRQoL. A consecutive sample from one hospital in China was used and 328 patients were included in the cross-sectional study. These patients completed a face to face interview with medical students including the following outcomes: EQ5D, MCMQ and PANAS.
It is a well-conducted study, with interesting results. However, a up-to-date knowledge of the literature on coping, mood and QoL seems missing, what hampers the interpretation of the findings of this study.

Major
• The manuscript is in need of English revision. I would suggest a professional English writer to correct the manuscript to improve its readability and clarity.

Authors' response: The revised manuscript was proofread by proofreading services.

- What is the rational to include only patient with an expected survival time of at least 3 months?

Authors' response: Studies show that cancer patients may experience a steep decline in HRQoL during the last 3 months of life (Raijmakers, Zijlstra, van Roij et al., 2018). It is possible that the characteristics of coping strategies and its association with HRQoL in patients with an expected survival time of less than 3 months may have some differences from that in patients with an expected survival time of more than 3 months, as they may have different treatment and care goals and life plans. Therefore, we purposefully included only those with an expected survival time of at least 3 months to examine the relationship among coping, mood, and HRQoL.

Raijmakers NJH, Zijlstra M, van Roij J et al. Health-related quality of life among cancer patients in their last year of life: results from the PROFILES registry. Supportive Care in Cancer 2018.

- Is the main outcome HRQoL best measured by the EQ5D? This measure is not well validated in advanced cancer patients, see review of Roij, J van et al 2018 in Quality of Life Research

Authors' response: Thanks for the question and suggestion. We have addressed this as a limitation in the discussion. Although EuroQol 5-dimension was used to measure HRQoL among patients with

advanced cancer in a range of studies (Chouaid et al., 2013; Shen et al., 2018), more information on the measurement properties of the instrument is needed to be examined in patients with advanced cancer (van Roij et al., 2018).

Chouaid C, Agulnik J, Goker E et al. Health-Related Quality of Life and Utility in Patients with Advanced Non-Small-Cell Lung Cancer: A Prospective Cross-Sectional Patient Survey in a Real-World Setting. Journal of Thoracic Oncology 2013; 8: 997-1003.

Shen YJ, Wu B, Wang XH, Zhu J. Health state utilities in patients with advanced non-small-cell lung cancer in China. Journal of Comparative Effectiveness Research 2018; 7: 443-452.

van Roij J, Fransen H, van de Poll-Franse L et al. Measuring health-related quality of life in patients with advanced cancer: a systematic review of self-administered measurement instruments. Quality of Life Research 2018; 27: 1937-1955.

- I would strongly suggest to divide table 1 into two separate tables, one with only the background variables and one with the outcomes of the measurements. Now it is a huge table with many subgroups. Some subgroups are too small to report anyway.

Authors' response: Thanks for your suggestions. The original Table 1 is separated into two tables. The Table 1 in the revised manuscript presents the sample characteristics. The cross-tabulation between sample characteristics and outcome measures is presented in supplementary Table 1.

- To add to the previous point: I am wondering if the analysis of variance test as presented on page 15, line 17-34 is contributing to this paper. I would suggest to leave this out, especially as comparing subgroups was not the aim of the study and the subgroups have no real rational why they would differ on HRQoL. For example in different treatment groups it is clear that HRqOl can differ, but is this due to the treatment or due to selection bias?

Authors' response: Thanks for your suggestions. We agree that the associations between socio-demographic and clinical characteristics and HRQoL are not the aim of this study. The paragraph has been removed, but the correlates are controlled in the multivariate and mediation analyses.

Minor

- I would suggest to have a good look at literature, as the authors claim to be the first study to examine the relationship between coping, mood and QoL in advanced lung cancer. This previous study has done the same: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5160928/

Authors' response: Thanks for the question. Nipp et al. (2016) examined relationship between coping, mood, and QoL in advanced lung cancer, but the study only considered negative mood, and mood and QoL were treated as two independent outcomes of coping. The current adds to the knowledge by including both positive and negative mood, and testing the mediating role of positive and negative mood in the association between coping and HRQoL.

- Page 4, line 43 "two coping strategies .. are regarded as important in cancer pt. This reference is from 1987 and therefor outdated. Please update literature on coping strategies in cancer. More than 2 strategies are present

Authors' response: Literature on the two coping strategies among patients with life-threatening illness has been updated.

• It may help if you would include a flowchart of the inclusion of the patients: XX asked, 328 included with LC, of these 267 had advanced-stage LU and of them 261 had provided complete information. Please add the number of patients that were approached for the study in total and the number of patients who refused. This is helpful for interpretation of the generalizability.

Authors' response: Doctors from the inpatient unit of the department of chest-oncology medicine at a public hospital screened the eligible patients for the study using the inclusion and exclusion criteria. The exact response rate of the present study was not recorded case by case during the survey period. Based on clinical research experiences of lung cancer research in the same hospital setting (e.g., number of beds and the completed questionnaires), the response rate of the present study was estimated to be approximately 72%.

• In Table 1 Time of diagnosis does not add up to 261. Please indicate the missings with an asterisk

Authors' response: Thanks for noting the incompleteness. For time since diagnosis, the sum of number is not 261 due to missing data. An asterisk has been added in the Table 1.

• Please add information on how strong the correlation is, when reporting about is, as done on page 15, line 3-14. "Age was inversely….. from slight to severe."

Authors' response: We have added the description to indicate the strength of the correlation among coping, mood, and HRQoL (see 3.2). As mentioned before, the paragraph on socio-demographic and clinical correlates of mood and HRQoL has been removed in the main text.

Reviewer: 4
Reviewer Name: Ramses Sadek
Institution and Country: Augusta University, Georgia Cancer Center, USA
Please state any competing interests or state 'None declared': None

Please leave your comments for the authors below

For the Stepwise regression method, need to clarify is this regular stepwise (variables can enter and leave) of forward variable selection. I see more than one variable entered at a time which is not common.
Need to clarify.

Authors' response: Thanks for your question. The multivariate analyses were hierarchical regression, which built the models for each outcome measure by adding variables to a previous model at each step. In step one, gender, age, cancer stage, and covariates that were significantly correlated with mood and HRQoL (i.e., financial burden, lung cancer type, received radiotherapy) were entered; In step two, confrontation and resigned acceptance were entered; In step three, positive and negative mood were entered. We have corrected this in the "data analysis" section.

VERSION 2 – REVIEW

REVIEWER	Laurie Steffen Wake Forest School of Medicine USA
REVIEW RETURNED	29-Aug-2018

GENERAL COMMENTS	Overall, authors have been responsive to previous review. However, I have two major concerns remaining. The first is that it

	is still unclear in the Introduction how you are conceptualizing these forms of coping and how they functionally similar or distinct from other forms of coping (some of which are cited as supporting background). The second is that it is unclear which items were used to assess coping. There seem to be discrepancies in how confrontation coping and resigned acceptance coping are described in the Methods and Discussion. If you are clear in the Intro how you conceptualize these forms of coping, clarify how your measurement aligns, and frame your discussion in line with how you actually assessed coping, I think the manuscript will tell a much tighter and more useful story of how these forms of coping may relate to qol through mood. Introduction: 1. I would recommend spending more time organizing your introduction. At present, it does not set up a clear framework and rationale for your study. One potential way to help organize the introduction: 1. Lung cancer incidence 2. Stressors of diagnosis ("The diagnosis of lung cancer can result…" 3. QoL is impacted and important to understand because of its prognostic value and endpoint for tx in and of itself ("QoL is significantly affected in pts with [please cite literature on lung cancer pts having worse qol than other solid tumors]…"Qol has prognostic value and is a main focus of tx given poor survival…") 4. How pts cope with illness may be a modifiable factor that contributes to qol 5. Types of coping and their relation to qol 6. Mood as mediator of specific forms of coping… 2. In the Introduction, please describe how resigned acceptance and confrontation are conceptually similar to other forms of coping (e.g., is confrontation conceptually similar to active coping? Is resigned acceptance conceptually similar to behavioral disengagement?) and in doing so explain how this conceptual work informed your specific hypotheses. 3. Please further clarify resigned acceptance – it does not seem to be just accepting a stressful situation without endeavors to alter it. Rather, it seems tied to pts feeling that there is nothing they can do/no hope, etc. In short, just emphasize the resignation aspect of it more for the reader. In doing so, it's much clearer why resignation's effects could be mediated by mood. Methods 1. Coping Measure. Please clarify whether acceptance-resignation was only assessed with 2 items, and whether confrontation was only assessed with one item from the original measure and one item you added. If the original measure that 5 items for acceptance-resignation and 8 items for confrontation, please clarify whether you administered the full scale and just selected 2 items for each because of internal reliability or whether you only administered 2 items for each. If you did only administered 2 items for each subscale, please justify. For example, per your Introduction, it seems that the confrontation subscale has items that assess social support seeking, information gathering, as well as cognitive reframing. Your items only assess information gathering. Further, in the Discussion, you note that you were not able to use the avoidance subscale of the MCMQ. It seems you perhaps did administer the full measure and then selected specific

	items? Similarly, on p. 24 in the Discussion, you state that confrontation "in the current study was characterized by attempts such as seeking information from various sources, asking for advice from family and clinicians, and conducting shared decision making" – I only see information seeking in your Methods section. Please clarify exactly which items were used and revise the Discussion accordingly. Results: 1. P 16. "Negative mood was negatively associated with more difficulty in all domains." – Did you mean to say higher negative mood was associated with more difficulty in all domains? Or, negative mood was negatively associated with all qol domains. Discussion: 1. P. 24. "Giving up control in the actual situation….could reduce positive mood, such as hope and inspiration…" Consider commenting on whether the PANAS assessed high vs. low-activation affect and whether assessing high vs. low activation affect might affect the relationships you observed. The example items you provided in the Methods section seem like high activation PA (as opposed to lower activation affect like content, peace, etc.) 2. After clarifying your coping measure in the Methods, you likely need to revise the clinical implications section of your Discussion. For example, if confrontation coping was limited to seeking information from magazines or the internet and did not include seeking information from providers or social support, does it suggest that information seeking might be helpful to the extent that patients are doing something to try to change their situation, but less helpful to the extent that information seeking reflects anxious behavior or to the extent that the information quality may be poor? What should we do for the patients who are resigned to their illness? Seems that they need activated/shown in their care what they can to do to improve their qol.

REVIEWER	Ramses Sadek Augusta University, USA
REVIEW RETURNED	21-Aug-2018

GENERAL COMMENTS	I would guard against the word "multivariate" as the analysis looks like a multiple regression. The methods as stated in the response is a forward stepwise regression.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 2
Reviewer Name: Laurie Steffen
Institution and Country: Wake Forest School of Medicine, USA
Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below
Overall, authors have been responsive to previous review. However, I have two major concerns remaining. The first is that it is still unclear in the Introduction how you are conceptualizing these forms of coping and how they functionally similar or distinct from other forms of coping (some of which are cited as supporting background). The second is that it is unclear which items were used to assess coping. There seem to be discrepancies in how confrontation coping and resigned acceptance coping

are described in the Methods and Discussion. If you are clear in the Intro how you conceptualize these forms of coping, clarify how your measurement aligns, and frame your discussion in line with how you actually assessed coping, I think the manuscript will tell a much tighter and more useful story of how these forms of coping may relate to qol through mood.

Authors' response: Thanks much for reviewing our article and constructive suggestions again! In this revision, we clarify the conceptualization of coping in the introduction, provide more details about the measurement in the methods, and link it with the explanation in the discussion.

Introduction:

1. I would recommend spending more time organizing your introduction. At present, it does not set up a clear framework and rationale for your study.

One potential way to help organize the introduction:

1. Lung cancer incidence
2. Stressors of diagnosis ("The diagnosis of lung cancer can result…"
3. QoL is impacted and important to understand because of its prognostic value and endpoint for tx in and of itself ("QoL is significantly affected in pts with [please cite literature on lung cancer pts having worse qol than other solid tumors]…"Qol has prognostic value and is a main focus of tx given poor survival…")
4. How pts cope with illness may be a modifiable factor that contributes to qol
5. Types of coping and their relation to qol
6. Mood as mediator of specific forms of coping…

Authors' response: Thanks for the suggestion. The introduction part is reorganized as following:
1st paragraph: lung cancer incidence, stressors of diagnosis, QoL is impacted and important to understand because of its prognostic value and endpoint for tx in and of itself
2nd paragraph: How pts cope with illness may be a modifiable factor that contributes to qol
3rd, 4th, 5th paragraph: Types of coping and their relation to qol
6th paragraph: Mood as mediator of specific forms of coping
7th paragraph: Aim of current study

2. In the Introduction, please describe how resigned acceptance and confrontation are conceptually similar to other forms of coping (e.g., is confrontation conceptually similar to active coping? Is resigned acceptance conceptually similar to behavioral disengagement?) and in doing so explain how this conceptual work informed your specific hypotheses.

Authors' response: Confrontation is defined as a set of coping strategies that involves seeking information and advice from various sources, seeking support from family and friends, and engaging in decision making. It is actively oriented.
Resigned acceptance is defined as a form of passive acceptance, in which individuals accept the stressful situation and give up endeavors or hope to deal with it. It is passively oriented. Resigned acceptance is similar with behavioral disengagement in terms of giving up endeavors to deal with it; However, behavioral disengagement focuses more on behavioral aspects, and resigned acceptance refers to giving up in either behavior or attitude.
We clarify the confrontation and resigned acceptance in the 2nd and 3rd paragraph.

3. Please further clarify resigned acceptance – it does not seem to be just accepting a stressful situation without endeavors to alter it. Rather, it seems tied to pts feeling that there is nothing they can do/no hope, etc. In short, just emphasize the resignation aspect of it more for the reader. In doing so, it's much clearer why resignation's effects could be mediated by mood.

Authors' response: Thanks for the suggestion. We clarify resigned acceptance and emphasize that resigned acceptance refers to accepting the stressful situation and giving up endeavors or hope to deal with it.

Methods

1. Coping Measure. Please clarify whether acceptance-resignation was only assessed with 2 items, and whether confrontation was only assessed with one item from the original measure and one item you added. If the original measure that 5 items for acceptance-resignation and 8 items for confrontation, please clarify whether you administered the full scale and just selected 2 items for each because of internal reliability or whether you only administered 2 items for each. If you did only administered 2 items for each subscale, please justify. For example, per your Introduction, it seems that the confrontation subscale has items that assess social support seeking, information gathering, as well as cognitive reframing. Your items only assess information gathering. Further, in the Discussion, you note that you were not able to use the avoidance subscale of the MCMQ. It seems you perhaps did administer the full measure and then selected specific items?
Similarly, on p. 24 in the Discussion, you state that confrontation "in the current study was characterized by attempts such as seeking information from various sources, asking for advice from family and clinicians, and conducting shared decision making" – I only see information seeking in your Methods section. Please clarify exactly which items were used and revise the Discussion accordingly.

Authors' response: The current study assessed with full scale of MCMQ (19 items). The original MCMQ had 18 items, and we added one item in the confrontation subscale. The avoidance subscale of MCMQ was not included in the analysis due to the low reliability. The acceptance-resignation subscale has 5 items, such as "there is nothing you can do about your illness", "you don't care what happens to you", and "just feel like giving in to your illness." The confrontation subscale has 9 items, such as "obtained information through books, magazines, and newspapers in the past several months", "try to talk about your illness with friends or relatives", "be involved in decisions regarding your treatment." The confrontation subscale reflects active coping strategies which assessed actively seeking information and advice from various sources, seeking support from family and friends, and being involved in decision making (Feiel, Strack, & Nagy, 1987).
We revise the illustration of confrontation in introduction, method, and discussion part to make it more consistent.

Results:

1. P 16. "Negative mood was negatively associated with more difficulty in all domains." – Did you mean to say higher negative mood was associated with more difficulty in all domains? Or, negative mood was negatively associated with all qol domains.

Authors' response: It is corrected accordingly in the text ("Negative mood was associated with more difficulty in all domains of HRQOL").

Discussion:

1. P. 24. "Giving up control in the actual situation….could reduce positive mood, such as hope and inspiration…" Consider commenting on whether the PANAS assessed high vs. low-activation affect and whether assessing high vs. low activation affect might affect the relationships you observed. The example items you provided in the Methods section seem like high activation PA (as opposed to lower activation affect like content, peace, etc.)

Authors' response: Thanks for the suggestion. A comment on high- vs. low-activated affect is provided in the discussion. PANAS mainly measured the high-activated affect. It is possible that

giving up attempt and hope may induce high-activated negative mood (e.g., distressed, scared, ashamed), rather than the high-activated positive mood (e.g., active, alert, interested). However, further study is suggested to investigate the relationship between resigned acceptance and low-activated mood, for instance, if low-activated positive mood (e.g., peace, calm) may emerge by accepting the advanced cancer despite in a passive way.

2. After clarifying your coping measure in the Methods, you likely need to revise the clinical implications section of your Discussion. For example, if confrontation coping was limited to seeking information from magazines or the internet and did not include seeking information from providers or social support, does it suggest that information seeking might be helpful to the extent that patients are doing something to try to change their situation, but less helpful to the extent that information seeking reflects anxious behavior or to the extent that the information quality may be poor? What should we do for the patients who are resigned to their illness? Seems that they need activated/shown in their care what they can to do to improve their qol.

Authors' response: Thanks for the suggestion. We revise the clinical implications section in the discussion.
Confrontation is defined in the introduction section (response to Question 2 related to Introduction). It is not limited to seeking information, but excessive information- or treatment-seeking behaviors, may reflect the anxiety and fear. Practitioners is suggested to pay attention to the excessive information- or treatment-seeking behaviors, and help relieve anxiety and fear among patients.
To work with patients who resigned in the situation, practitioners may help them to regain a sense of control and develop constructive responses. Support from family and a positive environment may also help to relieve the fears and fatalistic attitude (Hamilton et al., 2017).
Overall, early palliative care may be integrated into standard oncology care, which is suggested to facilitate adaptive coping, reduce emotional distress, and improve quality of life in patients with advanced cancer.

Hamilton, J. B., Worthy, V. C., Moore, A. D., Best, N. C., Stewart, J. M., & Song, M.-k. (2017). Messages of Hope: Helping Family Members to Overcome Fears and Fatalistic Attitudes Toward Cancer. Journal of Cancer Education, 32(1), 190-197. doi:10.1007/s13187-015-0895-z

Reviewer: 4
Reviewer Name: Ramses Sadek
Institution and Country: Augusta University, USA
Please state any competing interests or state 'None declared': None Declared

Please leave your comments for the authors below
I would guard against the word "multivariate" as the analysis looks like a multiple regression. The methods as stated in the response is a forward stepwise regression.

Authors' response: Thanks for the clarification. We revised the wording in method part as "hierarchical, multiple, linear regression analyses."

VERSION 3 – REVIEW

REVIEWER	Laurie Steffen Wake Forest School of Medicine
REVIEW RETURNED	09-Dec-2018

GENERAL COMMENTS	Thank you for the opportunity to review this revised manuscript. Authors have responded well to the concern about coping measurement and description. It is now much clearer! Now that it is clearer how coping was measured and conceptualized, the manuscript mostly needs minor editing and proofing throughout. I advise the following edits to the Discussion for clarity. 1. Although I appreciate the attempt to respond to my prior comment about the PANAS, recommend slight edits and moving it to Limitations. The section you added on page 25 "moreover, it should be noted…" should be revised to make it clearer what the issue with the PANAS was as it relates to resigned acceptance (i.e., that because the PANAS assessed high-activated positive affect, you were unable to assess whether resigned acceptance is related to higher low-activated positive affect). This could be achieved by paring down what you have written to "The PANAS mostly measured high activated positive and negative affect. Further study is needed to investigate the relationship between resigned acceptance and low-activated positive mood (e.g., peace, calm)." 2. Recommend structuring last paragraph of the Discussion so that strategies/clinical implications are grouped by intervention level. Right now, strategies that are appropriate for mental health providers (e.g., forms of psychotherapy such as Acceptance and Commitment Therapy) are intermixed with strategies for "practitioners", which I took to mean oncology providers (oncologists, Pas, NPs). In case it's not clear what I'm asking, based on your pieces in your Discussion, it seems you are essentially trying to say that 1) oncology providers may need to attend more to how patients are coping; 2) while fostering realistic expectations for treatment/prognosis, oncology providers should watch for resigned acceptance and help patients regain a sense of what they can still do; 3) when patients are engaging in excessive information seeking (i.e., part of confrontation coping), oncology providers should be aware that it might signal underlying anxiety and make sure patients have appropriate mental health care and support. Mental health providers may help address coping strategies, mood, and quality of life through evidence-based interventions (ACT)…early integrated palliative care is a comprehensive, evidence-based approach. Perhaps grouping your suggestions in some similar way would help the flow of your last paragraph.

VERSION 3 – AUTHOR RESPONSE

Reviewer: 2
Reviewer Name: Laurie Steffen
Institution and Country: Wake Forest School of Medicine
Please state any competing interests or state 'None declared': None declared

Please leave your comments for the authors below
Thank you for the opportunity to review this revised manuscript. Authors have responded well to the concern about coping measurement and description. It is now much clearer!
Now that it is clearer how coping was measured and conceptualized, the manuscript mostly needs minor editing and proofing throughout. I advise the following edits to the Discussion for clarity.

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Response: Thanks for the suggestion. The discussion of limitation of PANAS has been moved to the limitation part.

2. Recommend structuring last paragraph of the Discussion so that strategies/clinical implications are grouped by intervention level. Right now, strategies that are appropriate for mental health providers (e.g., forms of psychotherapy such as Acceptance and Commitment Therapy) are intermixed with strategies for “practitioners”, which I took to mean oncology providers (oncologists, Pas, NPs).
In case it’s not clear what I’m asking, based on your pieces in your Discussion, it seems you are essentially trying to say that 1) oncology providers may need to attend more to how patients are coping; 2) while fostering realistic expectations for treatment/prognosis, oncology providers should watch for resigned acceptance and help patients regain a sense of what they can still do; 3) when patients are engaging in excessive information seeking (i.e., part of confrontation coping), oncology providers should be aware that it might signal underlying anxiety and make sure patients have appropriate mental health care and support. Mental health providers may help address coping strategies, mood, and quality of life through evidence-based interventions (ACT)…early integrated palliative care is a comprehensive, evidence-based approach. Perhaps grouping your suggestions in some similar way would help the flow of your last paragraph.

Response: Thanks much for the thoughtful suggestion. The implications part has been re-structured to clarify the recommendations for different practitioners (oncology providers, mental health providers, multi-disciplinary providers).

VERSION 4 – REVIEW

REVIEWER	Laurie Steffen Wake Forest School of Medicine USA
REVIEW RETURNED	10-Jan-2019

GENERAL COMMENTS	Thank you for your work on iteratively revising this manuscript to address concerns. No further concerns.