PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	A cross-sectional study of the quality of life in Chinese inpatients with lung cancer
AUTHORS	Gu, Wen Xu, Yan-Min Zhong, Baoliang

VERSION 1 - REVIEW

REVIEWER	Mariusz Chabowski
REVIEW RETURNED	07-Oct-2017

GENERAL COMMENTS	I reviewed the paper titled „A cross-sectional study of the quality of life in Chinese inpatients with lung cancer" and it is very well-written and ready for publication.

REVIEWER	Alix Hall
REVIEW RETURNED	17-Nov-2017

GENERAL COMMENTS	This was a cross-sectional study aimed at identifying psychosocial characteristics associated with poor QoL in Chinese lung cancer patients. This is an interesting study that is well written and explained. The question is clear and interesting and the methods are appropriate. The authors also interpret their results within the limitations of their study. I only have a few suggested changes to help strengthen this paper. 1. Please provide details in the methods section about the normative data that was used to compare with the study sample. 2. Do the authors believe that it is possible that their small sample size may have impacted their ability to identify significant characteristics associated with QoL? There were quite a few predictors and only a small sample to test these in. Please consider the lack of power in the limitations section of the paper. 3. In table 1 please provide the number and percentages of patients for all categories of demographic details (i.e. all levels of marital status). This will allow readers to understand the full profile of the sample.

REVIEWER	Marianne Heins
REVIEW RETURNED	08-Jan-2018

GENERAL COMMENTS	This paper describes a survey that examined the quality of life (QOL) in inpatients with lung cancer treated in two large Chinese hospitals. It also explored the demographic, clinical, and psychosocial factors associated with QOL. It is generally quite well written, but the message that QOL is poor in these patients is not very new or surprising and the predictors of QOL that the study examined partly overlap with QOL itself. Introduction I am confused by the rationale for this study as described of the introduction. What is exactly the problem you are trying to solve? It is stated that it is important to examine the level and predictors of QOL in cancer patients to develop more effective clinical interventions. First, the term clinical interventions is ambiguous. Does it refer to anticancer treatments? Or interventions aimed at the physical and psychological side effects of anticancer treatments? Please describe how more knowledge on QOL could help to develop these interventions. In the discussion section the authors write that 'quality of life should be prioritised over quantity of life in cancer treatment practice'. According to the theory of shared decision making (Elwyn, Journal of General Internal Medicine, 2012) doctors and patients should discuss together "what matters most" to patients. This can be quantity of life, if patients for example want to do everything to be present at the wedding of their son/daughter, or quantity of life, if they do not want to spend the time they have left sick or in hospital. This trade-off between quality and quantity of life could fit excellently in the introduction and would support the importance of QOL in lung cancer patients. Next, the introduction contains references to several studies that already measured QOL and its predictors in Chinese lung cancer patients. Please describe in more detail why the current study is needed and what it adds to the existing studies. It is stated that only very few of these studies focused on psychosocial predictors of QOL. Please elaborate, which psychosocial factors would be The study was conducted in hospitalised patients, who are more likely to have a poor QOL than patients who are not hospitalised. This should be mentioned and it should be explained why this group was chosen. Methods An overview of the explanatory factors, divided into demographic, clinical and psychosocial would be very helpful. This could be provided in a separate table, or by clearly separating these categories in the methods section (e.g. with subheadings) and in table 1. Marital status, economic status and possibly also education could, and in my opinion should, be regarded as psychosocial factors. There is overlap between some of the explanatory factors and the outcome QOL. For example, performance status (clinical factor) is also part of physical QOL and depression and anxiety (psychosocial factors) are also part of psychological QOL. It is therefore not surprising that they are related to the outcome measure. These

	factors should not be used as predictors for the corresponding type of QOL. P 7 line 41 'following a careful review'; Was the review of the medical records and interview with patients and oncologist performed after patients completed the form? Then it should be 'followed by a careful review..'. Results The number of invited and included patients should be part of the results section, rather than the methods section. Please also describe the number of patients with lung cancer who were invited, to see whether the response in this group as lower than in other cancer types. How do you explain that a high performance status is related to a low physical and psychological quality of life? This is counterintuitive, especially for physical QOL. Please examine this further. Discussion Part of the literature mentioned in the discussion section would be more suitable in the introduction section, e.g. that diagnosis and treatment for lung cancer are very stressful and the QOL satisfaction model. As already mentioned, a clear separation between the different types of factors would be helpful. This separation could also be made more clearly in the discussion section. There are only 8 patients who were unmarried and 13 who are not receiving chemotherapy . These are very small numbers to support the conclusion that patients who are not married or patients receiving chemotherapy have a lower QOL. This conclusion should therefore be phrased more carefully. Tables - In table 1 please report numbers in all categories (male/female, married/not married, SES poor/middle/high etc).

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

I reviewed the paper titled, A cross-sectional study of the quality of life in Chinese inpatients with lung cancer" and it is very well-written and ready for publication.

Answer: Thank you very much for the review.

Reviewer: 2

1. Please provide details in the methods section about the normative data that was used to compare with the study sample.

Answer: The normative data are derived from a representative sample (N=1052) of Chinese adult residents. In this revised version, we have been briefly described this information in the Statistical analysis.

2. Do the authors believe that it is possible that their small sample size may have impacted their ability to identify significant characteristics associated with QoL? There were quite a few predictors and only a small sample to test these in. Please consider the lack of power in the limitations section of the paper.

Answer: Thanks very much. We agree with you. According to a paper published in Psychosom Med (Ref.), the minimum number of subjects per predictor required in multiple linear regression analyses is 10-15. We studied 16 candidate predictors in this study, but our sample size is 148. Therefore, the sample size of our study is relatively small, limiting the ability of our multiple linear regression model to identify more significant predictors of QOL. In the revised version of our paper, we have added this limitation to the “limitation paragraph”.

Ref.: Babyak MA. What you see may not be what you get: a brief, nontechnical introduction to overfitting in regression-type models. Psychosom Med. 2004;66(3):411-421.

3. In table 1 please provide the number and percentages of patients for all categories of demographic details (i.e. all levels of marital status). This will allow readers to understand the full profile of the sample.

Answer: We have provided these data accordingly.

Reviewer: 3

This paper describes a survey that examined the quality of life (QOL) in inpatients with lung cancer treated in two large Chinese hospitals. It also explored the demographic, clinical, and psychosocial factors associated with QOL. It is generally quite well written, but the message that QOL is poor in these patients is not very new or surprising and the predictors of QOL that the study examined partly overlap with QOL itself.

Answer: We highly appreciate your comments on our paper.

First, we agree that the finding of poor QOL in patients with lung cancer is not very new, but this study also revealed the significant association between psychosocial factors and QOL, which is rarely studied in previous studies in China. Further, open journals such as BMJ Open focus on scientific “soundness” of a study, not novelty or importance. The possible lack of novelty should not be an issue of our study.

Second, strictly speaking, it is not correct to say that performance status overlaps physical QOL and psychological factors overlap psychological QOL. QOL is the general well-being of individuals and groups, which usually includes subjective evaluations of both positive and negative aspects of life. Health-related QOL narrows QOL to aspects relevant to health. Therefore, physical and psychological QOL is a subjective sense of physical and psychological health.

We used the ECOG scale to assess the performance status, which is patients’ daily living abilities, including ability to care for themself, daily activity, and physical ability (walking, working, etc.). Based on this definition, we can speculate that performance status would be related to or influence physical QOL, but we can not say performance status partly overlaps physical QOL, because the former is an objective measure of daily living abilities (usually completed by oncologists through physical examination and observation), and the latter is subjective feelings. Briefly speaking, they may be correlated, but they are different constructs.

Psychological factors in our study included depressive and anxiety symptoms, two specific common mental health problems. Psychological QOL is the overall subjective sense of an individual’s positive (such as happiness) and negative mental health status, but not specific to negative emotion such as depression and anxiety. There is also no any component of the psychological QOL specific to

depression and anxiety. Similarly, depression/anxiety may influence psychological QOL, but this relationship does not mean that they partly overlap, because they are two different constructs.

Introduction

I am confused by the rationale for this study as described of the introduction. What is exactly the problem you are trying to solve? It is stated that it is important to examine the level and predictors of QOL in cancer patients to develop more effective clinical interventions. First, the term clinical interventions is ambiguous. Does it refer to anticancer treatments? Or interventions aimed at the physical and psychological side effects of anticancer treatments? Please describe how more knowledge on QOL could help to develop these interventions.

Answer: The direct goal of this study is to investigate the level and predictors of QOL in patients with lung cancer, and the findings from this study would help develop more effective clinical interventions. The term “clinical interventions” seems unclear here. In this revised version of our paper, we explained the objective of this study as follows.

“Cancer treatment is challenging, because many physical and psychosocial problems are present at all stages of the disease but conventional treatment for cancer such as chemotherapy focuses on addressing the physical dimensions of cancer (i.e., stopping or slowing the growth of cancer cells). Given that QOL is a comprehensive assessment of clinical outcome, examining the level and predictors of QOL in patients with cancer is therefore essential in developing measures to improve quality of care and treatment outcomes”.

In the discussion section the authors write that ‘quality of life should be prioritised over quantity of life in cancer treatment practice’. According to the theory of shared decision making (Elwyn, Journal of General Internal Medicine, 2012) doctors and patients should discuss together “what matters most” to patients. This can be quantity of life, if patients for example want to do everything to be present at the wedding of their son/daughter, or quality of life, if they do not want to spend the time they have left sick or in hospital. This trade-off between quality and quantity of life could fit excellently in the introduction and would support the importance of QOL in lung cancer patients.

Answer: Thanks very much. These points raised by you are correct. Our statement is too arbitrary. This sentence has been rewritten as below.

“Therefore improving the QOL of patients with limited life expectancy should be a primary concern in lung cancer treatment practice”.

Next, the introduction contains references to several studies that already measured QOL and its predictors in Chinese lung cancer patients. Please describe in more detail why the current study is needed and what it adds to the existing studies. It is stated that only very few of these studies focused on psychosocial predictors of QOL. Please elaborate, which psychosocial factors would be.

Answer: We carefully reviewed these available studies and found only one reported the significant relationship between social support and the global QOL in Chinese lung cancer patients. The sentence has been re-written as below in this revision.

“However, compared to international studies, very few of them focused on the roles of psychosocial factors on QOL: only one reported the significant association between social support and the global QOL in patients with newly diagnosed lung cancer”.

The study was conducted in hospitalised patients, who are more likely to have a poor QOL than patients who are not hospitalised. This should be mentioned and it should be explained why this group was chosen.

Answer: This is a limitation of our study. In general, hospitalized patients should have poorer QOL than not hospitalized patients, but this comparison is not the focus of our study. In this revision, we discussed this limitation as below.

“Finally, we recruited patients with lung cancer from inpatient departments of large general hospitals only, outpatients of general hospitals and primary care patients were not included, potentially influencing the representativeness of the sample of patients with lung cancer. We need to be cautious in generalizing findings of the present study to all patients with lung cancer”.

Methods

An overview of the explanatory factors, divided into demographic, clinical and psychosocial would be very helpful. This could be provided in a separate table, or by clearly separating these categories in the methods section (e.g. with subheadings) and in table 1.

Answer: In Assessments, we have used separated paragraphs to describe the three types of factors. In the footnote of Table 1, a detailed explanation on the three types of factors has been added.

Marital status, economic status and possibly also education could, and in my opinion should, be regarded as psychosocial factors.

Answer: Thank you. In the literature, it is more common to categorize marital status, economic status and education as demographic factors.

There is overlap between some of the explanatory factors and the outcome QOL. For example, performance status (clinical factor) is also part of physical QOL and depression and anxiety (psychosocial factors) are also part of psychological QOL. It is therefore not surprising that they are related to the outcome measure. These factors should not be used as predictors for the corresponding type of QOL.

Answer: Thanks. As I explained above, performance status and physical QOL, and depression/anxiety and psychological QOL, are different constructs. They are correlated but not overlapped. In the literature, it is very common to find studies that assess the relationship between performance status, depression, anxiety and QOL (e.g., Ref.1-3).

Ref.1: Brenes GA. Anxiety, depression, and quality of life in primary care patients. Prim Care Companion J Clin Psychiatry. 2007;9(6):437-43.

Ref.2: Scévola L, Sarudiansky M, Lanzillotti A, et al. To what extent does depression influence quality of life of people with pharmacoresistant epilepsy in Argentina? Epilepsy Behav. 2017;69:133-138.

Ref.3: Prigerson HG, Bao Y, Shah MA, et al. Chemotherapy Use, Performance Status, and Quality of Life at the End of Life. JAMA Oncol. 2015;1(6):778-84.

P 7 line 41 ‘following a careful review’; Was the review of the medical records and interview with patients and oncologist performed after patients completed the form? Then it should be ‘followed by a careful review..’.

Answer: Thanks a lot. It is wrong to use “following” here. We have replaced it with “followed by”.

Results

The number of invited and included patients should be part of the results section, rather than the methods section. Please also describe the number of patients with lung cancer who were invited, to see whether the response in this group as lower than in other cancer types.

Answer: We have provided these figures in the results section. The response rate of lung cancer patients is higher than that of the whole sample of cancer patients, 82.7% (148/179) vs. 70.3% (517/735).

How do you explain that a high performance status is related to a low physical and psychological quality of life? This is counterintuitive, especially for physical QOL. Please examine this further.

Answer: Higher ECOG score denotes poorer performance and higher QOL score indicates better QOL. Therefore ECOG score is negatively correlated with QOL score. Our finding on their relationships is reasonable. Details of the ECOG scale have been provided in the footnote of Table 1.

Discussion

Part of the literature mentioned in the discussion section would be more suitable in the introduction section, e.g. that diagnosis and treatment for lung cancer are very stressful and the QOL satisfaction model.

Answer: Thanks. We think it is more appropriate to put the literature in the Discussion section, because citing the literature here can facilitate our explanation on the relationship between social support and QOL.

As already mentioned, a clear separation between the different types of factors would be helpful. This separation could also be made more clearly in the discussion section.

Answer: The 2nd, 3rd, and 4th paragraphs of Discussion focus on the relationships between QOL and demographic, clinical, and psychosocial factors, respectively. This separation is clear for the Discussion section.

There are only 8 patients who were unmarried and 13 who are not receiving chemotherapy. These are very small numbers to support the conclusion that patients who are not married or patients receiving chemotherapy have a lower QOL. This conclusion should therefore be phrased more carefully.

Answer: Many thanks for your comments. The small number of patients who were unmarried and not receiving chemotherapy is a limitation of our study. In this revision, we have added it as below.

“Further, due to the small number of patients who were unmarried patients (N=8) and not receiving chemotherapy (N=13), our findings on the relationships between QOL and marital status and treatment regimen might not be reliable. Large-scale studies are warranted to confirm these relationships”.

We have no revisions on the conclusions, because our conclusion focused on the poor QOL of patients with lung cancer and the association between psychosocial factors and poor QOL.

Tables

- In table 1 please report numbers in all categories (male/female, married/not married, SES poor/middle/high etc).

Answer: These figures have been added accordingly.

VERSION 2 – REVIEW

REVIEWER	Alix Hall
REVIEW RETURNED	10-Feb-2018

GENERAL COMMENTS	This is a cross-sectional survey study, assessing the QoL of lung cancer patients from China. It provides a comparison of QoL o lung cancer patients with Chinese normative data as well as identifying socio-demographic and disease characteristics associated with QoL. This is a well explained and justified paper. It provides important data that is currently not available. The authors consider the limitations and interpret their findings well within the constraints of these limitations. I have provided a few suggestions below to help improve the paper. Introduction • Some data describing the prevalence, incidence and survival rates of lung cancer in China would be helpful. Methods • Despite being published elsewhere it would be useful for the authors to provide some details about how patients were approached and recruited, how data collection was obtained (i.e. by a research assistant in the hospital, or interview conducted at home etc). • Were assumptions of linear regression assessed, such as multivariate normality and homogeneity? Did these assumptions hold? • Please state that human research ethics was obtained. Tables • It would be useful if the unadjusted coefficients and p-values are included in Table 3. It would also be useful to include 95% confidence intervals associated with the coefficients in Table 3.

REVIEWER	Marianne Heins
REVIEW RETURNED	03-Feb-2018

GENERAL COMMENTS	The authors answered my questions and improved the manuscript to my satisfaction.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 2

Introduction

• Some data describing the prevalence, incidence and survival rates of lung cancer in China would be helpful.

Reply: Thanks. In this revised version of our paper, we have described the epidemiology of lung cancer in China as below:

“In 2013, population-based cancer registration data estimated that the crude incidence and mortality rates of lung cancer in China were as high as 70.1 and 36.8 per 100000 respectively, and the two rates have been stable in recent years. Meanwhile, due to the poor quality of care and limited medical treatment for lung cancer, the overall five-year survival rate of lung cancer remains low in China (16.1%), particularly in rural regions (11.2%)”.

Methods

• Despite being published elsewhere it would be useful for the authors to provide some details about how patients were approached and recruited, how data collection was obtained (i.e. by a research assistant in the hospital, or interview conducted at home etc).

Reply: In this revision, we have provided more details on the inclusion of eligible subjects and data collection as below:

“Briefly, adult patients who were diagnosed with lung cancer and hospitalized in the two hospitals at the time of the survey were consecutively invited to participate in the study. Eligible subjects were those who were aware of the diagnosis of lung cancer (ascertained by histological examination), aged 18 years and above, and had the capacity to provide informed consent. We excluded patients who were too ill, had cognitive disorders (i.e., dementia), or had difficulties in communicating with others”.

“Data were collected in places of the hospitals that were deemed convenient and could provide reasonable privacy for respondents (oncologists’ office, sickroom, etc.). All patients independently and anonymously completed the questionnaires on demographic characteristics, HADS, SSRS, and WHOQOL-BREF. Trained investigators interviewed patients and their treating oncologists and reviewed medical records to collect data on clinical factors”.

• Were assumptions of linear regression assessed, such as multivariate normality and homogeneity? Did these assumptions hold?

Reply: Thank you. Our data met the four assumptions for multiple linear regression analysis. In this revision, we described the results of testing for these assumptions in the Statistical analysis as below:

“The assumptions of linearity, normality, homoscedasticity, and absence of multicollinearity for multiple linear regression analysis were tested prior to the formal analysis. Because there were no curvilinear relationships in scatterplots of outcome variables versus continuous independent variables, and no clear distribution patterns in scatterplots of residuals (errors between observed and predicted outcome values) versus predicted outcome values, our data met the assumptions of linearity and homoscedasticity. We also found a normal distribution of residuals for physical QOL (K-S statistic=0.064, P=0.20) and psychological QOL (K-S statistic=0.068, P=0.10) in the Kolmogorov-Smirnov test. Variance Inflation Factor (VIF) values of all independent variables ranged from 1.13 to 5.77, markedly below the critical threshold of 10, indicating a very low degree of multicollinearity among the variables”.

• Please state that human research ethics was obtained.

Reply: Thank you. According to the guideline to authors of BMJ Open, we have provided a separate section to describe the ethics approval of our study. This section can be found in page 24:

ETHICS APPROVAL

The Ethics Committee of Wuhan Mental Health Center approved the study protocol. The protocol including the methods was performed in accordance with the Declaration of Helsinki and the relevant ethical guidelines and regulations in China. Written informed consent was obtained from all participants.

Tables

• It would be useful if the unadjusted coefficients and p-values are included in Table 3. It would also be useful to include 95% confidence intervals associated with the coefficients in Table 3.

Reply: Unadjusted coefficients, their corresponding 95%CIs and P values have been provided in Table 3 of this revision.