Reviewer’s report

Title: The association of depressive symptoms, personality traits, and sociodemographic factors with Health-Related Quality of Life and Quality of Life in patients with advanced-stage lung cancer: an observational multi-center cohort study

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Reviewer: Lara N Traeger

Reviewer's report:

Thank you for the opportunity to review this manuscript. The authors report results of a cross-sectional observational study of sociodemographic, clinical, personality, mood and anxiety predictors of QOL and health-related QOL in newly diagnosed patients with advanced lung cancer who are initiating active treatment. The paper adds to the literature on risk factors for poor quality of life at the start of lung cancer treatment. Recommendations to strengthen the manuscript are provided below.

Main points

I recommend clarifying the authors' differentiation between HRQOL and QOL. The manuscript description, that "HRQOL measures only patients' feelings related to their health, while QOL also reflects additional concepts such as the environment and spirituality," suggests that HRQOL may be subsumed within QOL. It would be helpful to distinguish the two constructs, along with careful attention to measurement differences between general versus health-related versus disease-specific measures of quality of life and the purposes of each in research or clinical contexts.

The authors state that the aim of the paper is to evaluate the association of depression symptoms and personality traits with HRQOL. It would help to clarify whether they had a priori hypotheses about direction of these associations, given prior literature, or whether they considered this an exploratory study. It would also help to clarify this in reference to a priori considerations for statistical power.

Questions or concerns about the statistical plan: The abstract notes the use of backwards stepwise regression, but this is not addressed in the methods. Recommend explaining rationale for selecting this method with attention to any potential limitations. The introduction also states that age, PS, gender, education, and marital status have been associated with HRQOL in patients with lung cancer; so it would be helpful for the authors to explain why they selected only age and gender as a priori control variables and tested the remaining factors for statistical significance as the criterion for model entry. The authors also note a minimum sample size necessary for model building, which led them to first conduct simple regressions of each predictor and control variable with each outcome. However, it would be helpful to address the large number of analyses. Did the authors consider options for prioritizing or reducing analyses or adjusting for family-wise error? Might the authors also address the potential overlap of CESD items with psychological items in the QOL measures?

I recommend attending to clinical generalizations in the discussion, such as '(HR)QOL management is mandatory in patients with poor prognosis", or "physician awareness of depression symptoms…could stimulate early referral to a psychologist," given current national and regional guidelines and common available resources at cancer centers. At the same time, it would be helpful to have more attention to placing current results in context of existing research and next steps, including observational or
intervention research in lung and other related cancers. Given the number of analyses, it may be challenging to synthesize the results while having space to interpret them, but I felt it was somewhat confusing to have the discussion report on new follow-up analyses that were not addressed in the methods and results. The paragraphs that summarized the main results attended mainly to the statistical explorations, but the authors may consider how to strike more of a balance between those and implications.

Introduction
Were the data collected specifically for the current study? If not, what were the aims of PERSONAL and how did the current study aims fit into those? I recommend clarifying this in the text.

Methods and results
Would be helpful to include more information about study procedures. How were the current study measures administered? How was study eligibility confirmed? What was the source of the sociodemographic and clinical data that were collected for the study? Under clinical information, it would help to clarify what is meant by 'history' or how 'disease response' was measured. How was the NEO-FFI scored -raw scores used or transformation into T-score?

Tables 3 and 4 may be showing only the regression predictors that had statistically significant associations with the outcomes, and perhaps this is related to running backwards selection, but to fully understand which variables were tested in each model, the reader might have to review numerous online supplemental simple regression tables. The authors might consider other ways to present information about the models that were run.

I suggest clarifying support for using the CES-D in cancer, given the neurovegetative symptoms that could overlap with cancer and cancer treatment-related symptoms. The authors note that the CES-D and the NEO-FFI both have good psychometric properties, but it would help to clarify and cite which populations were used to establish the properties that they are referring to.

Discussion
Both the introduction and the discussion state that significant treatment side effects and adverse events impact QOL in patients, but it could be made clearer that the study focused on patients who had not yet started treatment (except possibly for those on second line treatment).

Minor points
The authors use an acronym (HR)QOL that might be referring to both HRQOL and QOL simultaneously. As his is not a common notation and may not reflect the authors stance that QOL and HRQOL are distinct constructs, it may help to avoid using it.

With respect to the minimal missing data observed in the study, I wasn't sure why the number of patients who completed the questionnaires, as shown in Figure 1, was higher than the sample sizes used to calculate the mean scores on the questionnaire subscales.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No
Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
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