

## LETTER OF REVIEWERS

Reviewer A:

Recommendation: Revisions Required

This study addresses a current and relevant issue. It is interesting and presents particular strengths, such as the sample size, the precise regression analyses with sociodemographic variables, and the conclusions supported by up-to-date literature. However, there are aspects that could be improved to enhance the study. These include the precision of the psychometric properties of the scales used and the justification of the procedures from the design phase. The discussion section could also be expanded.

Reviewer B:

Recommendation: Revisions Required

**Relevance:** High

**Novelty:** Low or very low

**Presentation and writing:** High

### Comments for authors:

Dear Authors,

Thank you for submitting your article to the Journal "Interacciones: Journal of Family, Clinical and Health Psychology", the following comments were made in order to improve your article, and in view of verifying the validity of the methodology, analysis and results found, please take into account in a timely manner each of the suggestions and comments made.

Title and Abstract:

1. What is your exposure and outcome variable? The title of the study states that depression, anxiety, stress, and emotional distress are the exposure factors associated with quality of life (Outcome). However, in the objective of your study, this relationship is inverse: associating quality of life with the factors. Please clarify. If changes are made after this review, this description should be standardized in the full manuscript.
2. Keywords: Verify that the keywords used are indexing terms, this can greatly increase your visibility as well as citation possibilities.

Introduction:

3. The introduction provides a good justification for the topic; however, there is a lot of redundant information and verbosity. I suggest reducing the introduction to a maximum of 500 words, using the most relevant citations related to your stated topic and the outcomes of interest. Many of these references can be used to contrast the discussion of your results. Generally, the introduction should follow the following structure:

- Problem
- Brief review of the literature on the stated topic.
- Knowledge gap to be studied
- Response to the GAP, i.e., the stated main objective and design to be used to answer this research question, as well as a brief description of the methodology used.

4. In the first paragraph of the introduction, first line describes the annual number of cases and deaths, but of which disease? please detail.

5. Regarding the last paragraph of the introduction, What is your main and secondary objectives?

#### Materials and methods:

6. I recommend adding a statement to the study design section stating that the Strobe Guidelines for Reporting this cross-sectional study were followed. Verify that all items in the guidelines are met in the manuscript, and I recommend adding a table in the supplementary material indicating compliance with each item.

7. In the last paragraph of the participants section, regarding the sample size, this may enter into the statistical analysis. Although it is indicated that the sample size was estimated using a Poisson regression model, the software, statistical package or formula used for this estimation is not specified. To ensure the transparency and reproducibility of the study, it is recommended to explicitly state whether any specialized software or online calculator was used, as well as the key commands or parameters used. This information is essential so that other researchers can verify or reproduce the calculation in similar studies.

8. Regarding the variables section, particularly the Emotional distress section. Although it is argued that the HADS can capture a broader construct of emotional distress, it would be useful to clarify more precisely the extent to which this measure differentiates and adds value to the constructs already assessed, especially if statistical analyses simultaneously include these variables. It is recommended that greater justification be provided for the inclusion of this transdiagnostic construct, or that its analytical integration be considered as a composite variable.

9. Regarding the covariables section, in the first paragraph, second line are reported the categorized ages, Justification for these age-related cut-off points, on what literature were they based?

10. In line 3, in the first paragraph of the covariates section, in relation to the type of care, what is the difference between outpatient and outpatient clinic?

11. Regarding the last line of the first paragraph of covariates, add the reference that supports the description of the clinical stages.

12. In the second paragraph of the covariables section, the comorbidity variable is described, with respect to which the transdiagnostic model is understood, however, given the relationship between the exposure variables and the covariates, it is important to assess collinearity in the model.

#### Statistical analysis:

13. To strengthen the validity of the results obtained using robust variance Poisson regression models, it is advisable to perform complementary analyses to assess the fit and stability of the model. These include collinearity analysis between independent variables, using variance inflation factors (VIFs) to rule out redundancy between variables; evaluation of relevant clinical interactions, which allow identification of potential effect-modifying variables; and sensitivity analysis, considering different categorizations of variables or alternative models, such as the log-binomial model. Regarding the selection of variables for multivariate models, the present study appears to have followed a statistical criterion ( $p$ -value  $< 0.05$  in the crude analysis); however, it is essential to clarify that the inclusion of covariates is also based on their clinical plausibility, their role as potential confounders, and empirical evidence from previous literature, defining the role of each of them. Furthermore, it is recommended that effect-modifying variables be explicitly assessed by incorporating interaction terms and comparing stratified models, with a  $p$ -value of  $< 0.10$  for interaction considered as an exploratory threshold. The systematic application of these procedures would contribute to a more robust and accurate interpretation of reported associations.

14. In the first paragraph of the section on Factors associated with mental health and quality of life, line 6-10. In the description of this variable of emotional distress, a less sensitive cut-off value (above 15) is described, clarifying and defining a single cut-off point used for statistical analysis. You refer to mild and moderate quality of life in your results. What were the cut-off points used and what literature are these cut-off points based on?

15. In the last paragraph of the statistical analysis section. I suggest adding how many multivariate models were created, and how the variables were entered into the model, what assumptions were evaluated if necessary, and what steps were followed to build them.

Results:

16. In the first paragraph of this section. It should be noted that the final sample size used in the analyses ( $n = 465$ ) coincides exactly with the estimated sample size reported. This can be clarified. This raises the possibility that the sample size calculation was performed post hoc rather than a priori. If this is the case, for future studies, we recommend clearly specifying whether the sample size calculation was performed prospectively and ensuring that this estimate guides the planning of data collection.

Discussion:

17. In the last paragraph, first line, I recommend using active voice.

Conclusions:

18. I suggest the authors review and optimize the conclusions section to improve its clarity and usefulness for the reader. It would be advisable to avoid repeating previously described results, focusing on synthesizing only the most relevant associations of the study. It is also suggested that the findings be explicitly linked to practical, policy, or clinical recommendations that can guide interventions in the care of cancer patients. Finally, given that this is a cross-sectional study, it would be pertinent to include a reflection on the implications for future research, considering the inherent limitations of the design regarding the possibility of establishing causal relationships.

Tables:

19. Check the relative frequencies in tables 1 and 2, some do not give 100%, and do not match the descriptions of results.

Interacciones seeks greater transparency in the review process and to provide credit to reviewers. If the editors decide to accept the manuscript, **would you like your name to appear as a reviewer of the article?**

Yes, I agree to have my name indicated as a reviewer.

## RESPONSE LETTER

Dear Reviewers,  
Warm greetings.

We sincerely appreciate the opportunity to resubmit our manuscript entitled “*Association between Quality of Life and Depressive Symptoms, Anxiety, Stress, and Emotional Distress in Peruvian Cancer Patients: A Cross-Sectional Study*” (ID-449), which was evaluated through a double-blind peer review process in the journal “*Interacciones*”.

We would like to express our sincere gratitude to the reviewers for their valuable observations and constructive comments, which have significantly contributed to improving the scientific, methodological, and editorial quality of the manuscript.

We have carefully reviewed each of the reviewers’ comments and have addressed all observations by making the corresponding revisions to the manuscript. For greater clarity, we have provided a detailed, point-by-point response to each comment, clearly indicating the changes made in the revised version of the manuscript.

Below, we present our responses organized accordingly:

Observation	Explanation	Section, page and paragraph
Reviewer A:		
These include the precision of the psychometric properties of the scales used and the justification of the procedures from the design phase	The rationale for the design and procedure applied was provided. Further information was provided on the psychometric properties of the tests.	Study design p. 3 and Variables pp. 3-5
The discussion section could also be expanded.	The discussion was restructured by improving its wording and avoiding redundancies.	Discussion (pp.8-9)
Reviewer B:		
Title and abstract		
What is your exposure and outcome variable? The title of the study states that depression, anxiety, stress, and emotional distress are the exposure factors associated with quality of life (Outcome). However, in the objective of your study, this relationship is inverse: associating quality of life with the factors. Please clarify. If changes are made after this review, this description should be standardized in the full manuscript.	The statistical analysis was modified: Quality of life (mental and physical components) was considered the outcome variable, while depressive symptoms, anxiety, perceived stress, and emotional distress were treated as exposure variables. Consequently, the study objective and related sections were modified to ensure conceptual and terminological consistency throughout the manuscript. The objective was modified by specifying the exposure and outcome variables: To determine the association between depressive symptoms, anxiety, stress, and emotional distress (exposures) and quality of life (outcome) in Peruvian patients with cancer.	Abstract (p.1.) Background (p. 3 párr. 8) Study design (p. 7) Statistical analysis (p.5 párr. 1 – 3)
2. Keywords: Verify that the keywords used are indexing terms, this can greatly increase your visibility as well as citation possibilities.	The keywords were replaced with terms from the UNESCO Thesaurus.	keywords (p. 1)
Background:		
3. The introduction provides a good justification for the topic; however, there is a lot of redundant information and verbosity. I suggest reducing the introduction to a maximum of 500 words, using the most relevant citations related to your stated topic and the outcomes of	The introduction was reduced and restructured following the suggested outline.	Background (p. 1-3)

<p>interest. Many of these references can be used to contrast the discussion of your results. Generally, the introduction should follow the following structure:</p> <ul style="list-style-type: none"> <li>- Problem</li> <li>- Brief review of the literature on the stated topic.</li> <li>- Knowledge gap to be studied</li> <li>- Response to the GAP, i.e., the stated main objective and design to be used to answer this research question, as well as a brief description of the methodology used.</li> </ul>		
<p>4. In the first paragraph of the introduction, first line describes the annual number of cases and deaths, but of which disease? please detail.</p>	<p>The quote has been corrected.</p>	<p>Background (p.3 párr. 1)</p>
<p>5. Regarding the last paragraph of the introduction, What is your main and secondary objectives?</p>	<p>The main objective was corrected and two secondary objectives were specified: To determine the association between educational level, type of cancer, and clinical stage and mental health problems in Peruvian cancer patients. To analyze the comorbidity of mental health problems and their association with the quality of life of Peruvian cancer patients.</p>	<p>Background (p.3, párr. 8)</p>
<p>Methods</p>		
<p>6. I recommend adding a statement to the study design section stating that the Strobe Guidelines for Reporting this cross-sectional study were followed. Verify that all items in the guidelines are met in the manuscript, and I recommend adding a table in the supplementary material indicating compliance with each item.</p>	<p>The use of STROBE guidelines for cross-sectional studies was added. <a href="https://www.strobe-statement.org/">https://www.strobe-statement.org/</a></p>	<p>Study design (p. 3)</p>
<p>7. In the last paragraph of the participants section, regarding the sample size, this may enter into the statistical analysis. Although it is indicated that the sample size was estimated using a Poisson regression model, the software, statistical package or formula used for this estimation is not specified. To ensure the transparency and reproducibility of the study, it is recommended to explicitly state whether any specialized software or online calculator was used, as well as the key commands or parameters used. This information is essential so that other researchers can verify or reproduce the calculation in similar studies.</p>	<p>The statistical software used and the considerations taken into account to obtain the sample size were specified.</p>	<p>Participants (p. 3)</p>
<p>8. Regarding the variables section, particularly the Emotional distress section. Although it is argued that the</p>	<p>The simultaneity of the construct of emotional distress was specified, and its inclusion as transdiagnostic was justified.</p>	<p>Variables (p. 4, párr. 4 - 6)</p>

<p>HADS can capture a broader construct of emotional distress, it would be useful to clarify more precisely the extent to which this measure differentiates and adds value to the constructs already assessed, especially if statistical analyses simultaneously include these variables. It is recommended that greater justification be provided for the inclusion of this transdiagnostic construct, or that its analytical integration be considered as a composite variable</p>		
<p>9.Regarding the covariables section, in the first paragraph, second line are reported the categorized ages, Justification for these age-related cut-off points, on what literature were they based?</p>	<p>The categorization of the covariates was justified.</p>	<p>Covariates (p. 5)</p>
<p>10. In line 3, in the first paragraph of the covariates section, in relation to the type of care, what is the difference between outpatient and outpatient clinic?</p>	<p>The request was specified.</p>	<p>Covariates (p. 5)</p>
<p>11. Regarding the last line of the first paragraph of covariates, add the reference that supports the description of the clinical stages.</p>	<p>The request was specified.</p>	<p>Covariates (p. 5)</p>
<p>12. In the second paragraph of the covariables section, the comorbidity variable is described, with respect to which the transdiagnostic model is understood, however, given the relationship between the exposure variables and the covariates, it is important to assess collinearity in the model.</p>	<p>Multicollinearity was assessed using VIF, and we structured the analyses according to the conceptual model, estimating separate models for specific symptoms of the disorder, emotional distress, and comorbidity, in order to avoid collinearity. The three models represent complementary perspectives derived from a single conceptual framework, rather than alternative specifications of the same model. Although Poisson regression was used for the main analyses, multicollinearity was assessed independently of the distribution of the outcomes using linear models, as collinearity refers to the relationship between predictors.</p>	<p><b>Methods:</b> Statistical analysis (p. 5, párr. 1-2)</p>
<p>Statistical analysis</p>		
<p>13.To strengthen the validity of the results obtained using robust variance Poisson regression models, it is advisable to perform complementary analyses to assess the fit and stability of the model. These include collinearity analysis between independent variables, using variance inflation factors (VIFs) to rule out redundancy between variables; evaluation of relevant clinical interactions, which allow identification of potential effect-modifying variables; and sensitivity analysis, considering different</p>	<p>Three complementary regression models were specified based on the conceptual framework of the study: a model with specific symptoms (depression, anxiety and stress), a transdiagnostic model focused on emotional distress and a model that assessed symptom comorbidity as an indicator of cumulative burden. Collinearity among independent variables was assessed using variance inflation factors (VIF), with values below 5 observed in all fitted models. Clinically plausible interactions were also explored, particularly</p>	<p><b>Statistical analysis</b> (p. 6, parr 3 y 4)</p>

<p>categorizations of variables or alternative models, such as the log-binomial model. Regarding the selection of variables for multivariate models, the present study appears to have followed a statistical criterion (p-value &lt; 0.05 in the crude analysis); however, it is essential to clarify that the inclusion of covariates is also based on their clinical plausibility, their role as potential confounders, and empirical evidence from previous literature, defining the role of each of them. Furthermore, it is recommended that effect-modifying variables be explicitly assessed by incorporating interaction terms and comparing stratified models, with a p-value of &lt;0.10 for interaction considered as an exploratory threshold. The systematic application of these procedures would contribute to a more robust and accurate interpretation of reported associations.</p>	<p>the potential modifying effect of sex on the association between emotional distress and physical and mental quality of life; however, no modification of the effect was found. Furthermore, sensitivity analyses were performed using log-binomial models, the results of which were consistent in direction and magnitude with those obtained using Poisson regression with robust variance. The selection of covariates was based not only on statistical criteria but also on clinical plausibility and previous evidence.</p>	
<p>14. In the first paragraph of the section on Factors associated with mental health and quality of life, line 6-10. In the description of this variable of emotional distress, a less sensitive cut-off value (above 15) is described, clarifying and defining a single cut-off point used for statistical analysis. You refer to mild and moderate quality of life in your results. What were the cut-off points used and what literature are these cut-off points based on?</p>	<p>A single cut-off point was used for emotional distress (<math>\geq 11</math>), chosen to improve the specificity of clinically relevant distress in cancer patients; and for quality of life, standardized clinical cut-off points are not available; therefore, a distribution-based approach using tertiles was applied, which were subsequently dichotomized for analytical purposes.</p>	<p><b>Statistical analysis</b> (p. 6, parr 3)</p>
<p>15. In the last paragraph of the statistical analysis section. I suggest adding how many multivariate models were created, and how the variables were entered into the model, what assumptions were evaluated if necessary, and what steps were followed to build them</p>	<p>In response to this suggestion, the last paragraph of the statistical analysis section was expanded to detail the process of constructing the multivariate models. Following the conceptual framework presented in Figure 1, three independent multivariate models were constructed to assess the association between mental health symptoms and quality of life. The first model included specific mental health symptoms (depression, anxiety, and stress), the second model assessed emotional distress as a transdiagnostic construct, and the third model analyzed symptom comorbidity as an indicator of cumulative burden. Variables were entered simultaneously into each model, adjusting for covariates selected according to statistical, clinical, and theoretical criteria.</p>	<p><b>Methods:</b> <b>Statistical analysis</b> Validity of the models (p. 5 y 6, parr. 2)</p>
<p>Results:</p>		
<p>16. In the first paragraph of this section. It should be noted that the final sample</p>	<p>The minimum required sample size was estimated a priori as 453 participants.</p>	<p>Statistical analysis:</p>

<p>size used in the analyses (n = 465) coincides exactly with the estimated sample size reported. This can be clarified. This raises the possibility that the sample size calculation was performed post hoc rather than a priori. If this is the case, for future studies, we recommend clearly specifying whether the sample size calculation was performed prospectively and ensuring that this estimate guides the planning of data collection.</p>	<p>Although 500 patients were initially recruited, the final analytical sample consisted of 465 participants after applying eligibility criteria and data quality checks, thus exceeding the minimum required sample size.</p>	<p>Participants (p. 3) Results Characteristics of the participants (p.6, parr. 1)</p>
<p>Discussion</p>		
<p>17. In the last paragraph, first line, I recommend using active voice.</p>	<p>It was corrected.</p>	<p>Strengths and limitations (p. 9) 1 parr. 1 line</p>
<p>18. I suggest the authors review and optimize the conclusions section to improve its clarity and usefulness for the reader. It would be advisable to avoid repeating previously described results, focusing on synthesizing only the most relevant associations of the study. It is also suggested that the findings be explicitly linked to practical, policy, or clinical recommendations that can guide interventions in the care of cancer patients. Finally, given that this is a cross-sectional study, it would be pertinent to include a reflection on the implications for future research, considering the inherent limitations of the design regarding the possibility of establishing causal relationships.</p>	<p>The conclusions section was optimized, linking conclusions to practical or clinical recommendations, and explaining the implications for future research.</p>	<p>Conclusions (p.10) -parr. 1</p>
<p>19. Check the relative frequencies in tables 1 and 2, some do not give 100%, and do not match the descriptions of results.</p>	<p>The frequencies in the tables were checked and found to match the transcripts of the results.</p>	<p>Tables and figures (p. 7-p.8)</p>