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**ARTICLE DETAILS**

<table>
<thead>
<tr>
<th>TITLE (PROVISIONAL)</th>
<th>Health-related quality of life in epilepsy and its associated factors among adult patients with epilepsy attending Mizan Tepi University Teaching Hospital, Southwest Ethiopia: a Cross-Sectional study</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUTHORS</td>
<td>Yesuf, Wudu; Hiko, Desta; Alemayehu, Eshetu; Kusheta, Samuel; Shita, Abel; Beyene, Melkamu</td>
</tr>
</tbody>
</table>

**VERSION 1 – REVIEW**

<table>
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<tr>
<th>REVIEWER</th>
<th>Quigg, Mark</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>University of Virginia, Neuro</td>
</tr>
<tr>
<td>REVIEW RETURNED</td>
<td>27-Sep-2023</td>
</tr>
</tbody>
</table>

**GENERAL COMMENTS**

This is a survey-based cross-sectional, non-controlled assessment of QOL in epilepsy in a unique setting (based in Ethiopia). Therefore, the main interest and novelty should lie in its comparisons with similar assessments in other countries, and the fine point should be that is adds rigor in comparison to previous assessments within the same country.

In general, problems with clarity, organization, and detail selection in Methods and Results require major revision. ESL requires editing. There is no approval from a research protection board. The omission of seizure frequency as a variable seems inappropriate.

Abstract:
- "Main outcome measure": please state the name of the main survey used in this study.
- “Results”: Are these subscales of one primary survey or separate surveys? See above. What statistical model was used in these comparisons? “beta” needs context.
- “Conclusions: The mean health-related QOL score of patients with epilepsy ….. is low”. Please make sure that we know what comparison group you use to make this determination. Low compared to what?

Introduction:
- It is overly long and repeats common information. I recommend diving right into the problem, presented in the 5th paragraph. The introduction should mention what the main findings were in the previous, presumptively inadequate Ethiopian surveys to properly set up the findings that will come with a more rigorous assessment. Some set up with common QOL deficits from other countries to set up comparisons b/t Ethiopia and outside Ethiopia is recommended.

Methods:
- Terminology: the standard for “anti-epileptic medications” has shifted to “antiseizure medications/ASM"
What is the design of this study? Prospective case collection, retrospective random case selection?

Was this study conducted with permission of an IRB? If not, it’s an automatic rejection.

Inclusion criteria: Is this a consecutive recruitment design? “Sample size” section below seems to contradict this assumption. Sample sizes belong in Results. Please explain what “an expectation that patients had a good experience on anti-epileptic drugs” means and how that formed an inclusion criteria. How was “epilepsy” determined (common workup/findings to ensure that the sample is homogeneous).

Exclusion: Sample/number excluded/reasons belong in Results. Here, I suggest “Exclusion criteria included inability to complete the forms due to medical illness or cognitive impairment.”

Data Collection: what languages was the QOLIE-31 conducted? What surveys were used for perceived stigma, self-esteem, physical activity? If the investigators’ own, please show what the questions were. This belongs in Data collection: Did family members help patients? Did patients themselves fill out forms, family members, or the investigators?”

I don’t see seizure frequency as a variable. This is a major omission. One would have expected that, in a study with no control population, that the opportunity to compare those with ongoing seizures with seizure-free individuals was an missed opportunity for a case-control structure.

Outcome variable: it’s sufficient to state that raw scores were adjusted as per standard recommendations of Vickrey ....

Measurement of the exposure variables: I see that the authors specify scales/surveys used later in Methods, whereas I had expected them earlier (as primed by the first paragraph in Data Collection). I suggest that any revision reorganize information so that the means of collecting surveys are tersely stated, the surveys themselves are presented next with a presentation of the primary outcome and dependent variables, and then the statistics. It’s confusing when these elements are cross-referenced presented several times in different locations.

Sample size: I’m confused by this paragraph. Earlier, the authors imply that this is a prospective, consecutive case collection design, but this section suggests that it’s a retrospective selection of cases pulled by a randomization scheme. Please be specific: I suggest the authors state the design first thing in Methods. And, please explain the need for a randomized case selection scheme.

Data quality management: translated what questionnaire? Translation and validation of the QOLIE should be moved to the primary outcome/primary survey section.

Data processing and management: consider condensing this section to telling us what the model was. Data hygiene procedures aren’t needed.

Results

I guess this is why the randomization scheme is confusing. The authors stated that 698 were selected, but only 340 analysed. The choice to throw away nearly ½ the sample doesn’t seem appropriate, whether justified by a randomization scheme or not.

Table 1. Why are some variables in Table 1 and others aren’t?

“One hundred sixty-nine (49.7%) of the respondents scored below the mean in overall HRQOL”. Are the authors comparing median vs mean QOLIE score here? Is there a comparison with a unregistered control group? I’m not sure what this serves.

“Factors Independently associated with HRQOL”: I think that the
authors constructed univariate regressions for all variables and included those in the multivariable regression those with p values <0.25. Where are those results?

Discussion
- “The overall mean of HRQOL among study participants was low and half of the respondents scored below the mean.” This statement appears recursive. The reader may expect that ½ of subjects would score below the mean value in a normal distribution. A low score means little without comparison to a control group or to a comparison of adjusted QOLIE scores between studies.
- A strength of this study is the diversity of citations to other studies. The authors, in the second paragraph, bring out these comparisons with a variety of other samples. I recommend at least summarizing these findings in Introduction to allow the implicit comparison made in the Discussion opening sentence. Is there a citation or several that sets the precedent for comparing adjusted scores across studies? Please cite them.
- The authors note that “being illiterate” was inversely… This raises the need to specify who and how surveys were obtained in this study.

This is a cross-sectional study of health-related quality of life and associated factors in 346 adult patients with epilepsy seen in a teaching hospital in southwest Ethiopia and treated with anti-seizure medications for at least 3 months. The authors used standardized questionnaires to assess each of the relevant variables in a relatively large number of patients. This is a topic of considerable interest, as there is relatively scarce information about factors impacting quality of life in patients with epilepsy in lower income countries, and this may help to guide interventions to improve quality of life in these countries.

The authors report an overall low QOL, using multivariable linear regression analysis to find that HRQOL was inversely associated with age, anxiety, depression, low self-esteem, perceived stigma, taking medication twice or more times per day, being illiterate, and having more than two seizures per year. Higher income, social support, and being seizure free for more than one year were associated with improved QOL. Overall the study seems well designed to specifically identify the impact of these factors on HRQOL, and the use of standardized tools in a large patients sample is definitely a strength.

Comments:
- The authors state throughout that the HRQOL was low at 55.6. In the discussion they state “low when compared with other findings.” It would be helpful to be more specific - compared to what (healthy population, epilepsy patients in other countries? Patients with other chronic diseases?) According to the QOLIE-31 scale, I believe that 50 is a T-score representing the mean HRQOL for a group of patients with epilepsy. In addition, the authors report that half of the patients scored below the mean. Is this not expected? I would appreciate a bit more information to better understand the interpretation of their findings.
- The discussion of HRQOL across the world could be more complete (for example, see Altaf Saadi et al., Quality of life in epilepsy—31 inventory (QOLIE-31) scores: A global comparison. Epilepsy & Behavior 2016 65:13-17.
- Overall, it seems surprising that the variables identified could be independent. In fact, throughout the discussion, possible relationships between these variables are hypothesized, and I believe that these may be of significant interest (for example, factors associated with increased stigma, effects of increased social support on other variables). Per the methods, the authors checked for multicollinearity and interaction terms between several of the variables, and did not find any significant issues. Could the authors please help me to understand how they chose which interaction terms to look at and the relevance of some of these factors possibly being associated?
- Might these possible interactions impact or in fact simplify the conclusions if associated covariates could be grouped together?
- If there are in fact no such associations, then I would suggest editing the discussion to identify reasons that might be independent, or other factors that might underlie the identified associations.

VERSION 1 – AUTHOR RESPONSE

Response to reviewer #1:
Thank you for your constructive comments. All the comments were addressed in the main text on the following points.

The comparisons with similar assessments in other countries and comparison to previous assessments in Ethiopia were thankfully added in this revision. Thank you for your critical observations and comments that problems with clarity and organization in the manuscript were revised. ESL is also edited thoroughly.

There is ethical approval of the research protocol obtained from the institution review board of the Institute of Health, Jimma University. This is now clearly indicated in this revision. The variable “seizure frequency” is not omitted from the study. It was indicated in the methods section and also presented in the results section as well as in the abstract as it was identified as one of the factors negatively affecting health-related quality of life.

Responses to specific comments by section are as follows:

Abstract:
- “Main outcome measure”: please state the name of the main survey used in this study.
  Response: thank you, the main survey used in this study as mentioned is the health-related quality of life in epilepsy 31 (QOLIE-31) inventories constituting seven subscales using an Institution-based cross-sectional study based on retrospective random cases selection. So, the QOLIE-31 Health Survey was used to assess health-related quality of life (HRQOL) in epilepsy.
- “Results”: Are these subscales of one primary survey or separate surveys? See above. What statistical model was used in these comparisons? “beta” needs context.
  Response: a multivariable linear regression model was used to identify factors associated with HRQOL in epilepsy and the “beta” coefficient indicated the slope and magnitude (R2) of the effect of the relationship between the exposure variables and HRQOL. We conducted the single primary survey “institution-based retrospective cross-sectional study” and measured all subscales using their respective tools. Once computed and recruited from simple linear regression, the subscales of the clinical and personal factors were analyzed in the final model as predictors of HRQOL. These are described in the methods section and not included in the abstract due to the journal formatting style.
  Thank you for the comment.
- “Conclusions: The mean health-related QOL score of patients with epilepsy ….. is low”. Please
make sure that we know what comparison group you use to make this determination. Low compared to what?

Response: "The mean health-related quality of life score of patients with epilepsy in Mizan Tepi University Teaching Hospital is low compared to other scores in Ethiopia and the global mean score." Thankfully this is expressly stated in the revised manuscript. Comparison with specific scores from other countries is discussed in the discussion section of this revision.

Introduction:

- It is overly long and repeats common information.

Response: thank you for the comment. We tried to improve the introduction section thoroughly focusing on deficits of HRQOLIE-31 studies and the need for this study.

Methods:

- Terminology: the standard for “anti-epileptic medications” has shifted to “anti-seizure medications/ASM”.

Response: thank you. This standard terminology expression is edited throughout the manuscript.

- What is the design of this study? Prospective case collection, retrospective random case selection?

Response: We used the institution-based cross-sectional study design based on retrospective random case selection. This is now clearly expressed in the revised manuscript and thank you for the comment.

- Was this study conducted with the permission of an IRB? If not, it's an automatic rejection.

Response: sorry for the lack of expression regarding ethical approval, but the study protocol was ethically approved by the institutional review board of the Institute of Health, Jimma University. Thank you for your outlook and this is now clearly expressed in the revised manuscript.

- Inclusion criteria: Is this a consecutive recruitment design? The "Sample size" section below seems to contradict this assumption. Sample sizes belong in Results. Please explain what "an expectation that patients had a good experience on anti-epileptic drugs" means and how that formed inclusion criteria. How was “epilepsy” determined (common workup/findings to ensure that the sample is homogeneous)?

Response: The sample selection is not a consecutive recruitment rather it is based on retrospective random case selection. Figure 736 is just to indicate the number eligible currently on follow-up in the psychiatry clinic, but this has to be best expressed in the study setting section, so it was taken to this section. So a sample size of 346 was selected using simple random sampling from a frame of total patients on follow-up (736). However, six were excluded. The expression “an expectation that patients had a good experience on anti-epileptic drugs” is used to indicate patients who have follow-up but as an unnecessary expression, it is corrected in this revision. Regarding the diagnosis/workup of the epilepsy, we included those known epileptic patients who have follow-up for at least 3 months and not the newly diagnosed patients. This is because it measures variables like drug adherence. It is therefore, the workup of epilepsy is not described in the manuscript. Thank you for your comments.

- Exclusion: Sample/number excluded/reasons belong in Results. Here, I suggest “Exclusion criteria included inability to complete the forms due to medical illness or cognitive impairment.”

Response: thank you, the expression as you suggested is corrected in the revised manuscript.

- Data Collection: In what language was the QOLIE-31 conducted? What surveys were used for perceived stigma, self-esteem, and physical activity? If the investigators own, please show what the questions were. This belongs in Data collection: Did family members help patients? Did patients themselves fill out forms, family members, or the investigators?"

Response: thank you for your comment. For all variables like QOLIE-31, perceived stigma, self-esteem, and physical activity, the surveys we used were QOLIE-31, the stigma of epilepsy scale, Rosenberg self-esteem scale and international physical activity questionnaire using interviewer-administered questionnaires translated to Amharic and record review technique for some variables using a checklist. All these surveys were described and cited under the measurement of variables section. As the survey is a face-to-face interview, the respondents were the epilepsy patients themselves and the questionnaires were filled out by the data collectors. So that only the person who has epilepsy was interviewed (not a relative or friend) because no one else knows how they feel and
this was indicated under the data collection section.

• I don’t see seizure frequency as a variable. This is a major omission. One would have expected that, in a study with no control population, the opportunity to compare those with ongoing seizures with seizure-free individuals was a missed opportunity for a case-control structure.
Response: the seizure frequency was not omitted. It was one of the variables studied in clinical and psychological factors. So the variable was listed under the variables section and the results section as well. It was identified as the associated factor of HRQOL in this study.

• Outcome variable: it’s sufficient to state that raw scores were adjusted as per the standard recommendations of Vickrey ….
Response: thank you, this is corrected as you suggested.

• Measurement of the exposure variables: I see that the authors specify scales/surveys used later in Methods, whereas I had expected them earlier (as primed by the first paragraph in Data Collection). I suggest that any revision reorganize information so that the means of collecting surveys are tersely stated, the surveys themselves are presented next with a presentation of the primary outcome and dependent variables, and then the statistics. It’s confusing when these elements are cross-referenced and presented several times in different locations.
Response: thank you for the comment. We tried to rearrange the logical sequence as you suggested in this revision. The scales under the data collection section were now taken and described under the measurement of exposure variables section. We reorganize the information as variables described first in the revised manuscript followed by data collection and data analysis.

• Sample size: I’m confused by this paragraph. Earlier, the authors imply that this is a prospective, consecutive case collection design, but this section suggests that it’s a retrospective selection of cases pulled by a randomization scheme. Please be specific: I suggest the authors state the design first thing in Methods. And, please explain the need for a randomized case selection scheme.
Response: you are right that the figure mentioned in the inclusion criteria to indicate the number eligible or total number of patients on follow-up at the psychiatry clinic is confusing with the sample size estimated. We took the figure to the study setting section and clearly described the study design as it was based on the retrospective random cases selection. So, we think it is clear now how our study was conducted concerning the selection of study participants. The calculated sample size was about half of the total population and to give an equal chance of participation in the study, we considered the randomization scheme and used a simple random sampling technique for the selection of samples from the sampling frame which is a list of patients on psychiatry follow-up for epilepsy from the registration logbook. Thank you for the comment.

• Data quality management: translated what questionnaire? Translation and validation of the QOLIE should be moved to the primary outcome/primary survey section.
Response: all the questionnaires were translated from English to Amharic. This is indicated in this revision. Translation and validation of the QOLIE-31 were taken to the measurement of the primary outcome variable section as you suggested. Thank you for the comments.

• Data processing and management: consider condensing this section to tell us what the model was. Data hygiene procedures aren’t needed.
Response: thank you, we have tried to condense the data analysis section focusing on the analysis model with its assumptions. The first paragraph is the assumptions fulfillment and the second paragraph is all about the model.

Results:

• I guess this is why the randomization scheme is confusing. The authors stated that 698 were selected, but only 340 were analysed. The choice to throw away nearly ½ the sample doesn’t seem appropriate, whether justified by a randomization scheme or not.
Response: thank you for the comment. The confusion point is the stated figure (698) under the inclusion criteria section which is the total study population eligible with the chance to be included in the study. We corrected the issue now in this revision. The selection of samples was based on a retrospective random selection of cases using simple random sampling from the study population.

• Table 1. Why are some variables in Table 1 and others aren’t?
Response: one of the reasons is to avoid redundancies of what is expressed in statements that have not been repeated in the table. However, the major reason is that the majority of continuous variables were analyzed for their measures of central tendency and dispersion and their mean with standard deviation were presented in statements. Only categorical variables were presented in the table.

• “One hundred sixty-nine (49.7%) of the respondents scored below the mean in overall HRQOL”. Are the authors comparing the median vs mean QOLIE score here? Is there a comparison with an unregistered control group? I’m not sure what this serves.

Response: this result doesn’t go in line with the study objective and is therefore omitted in this revision as you suggested. Thank you for the comment.

• “Factors Independently associated with HRQOL”: I think that the authors constructed univariate regressions for all variables and included those in the multivariable regression with p values <0.25. Where are those results?

Response: thank you for the comment. Table 2 presented multivariable regression results with variables included in the final model. Univariate analysis is used just to recruit variables for the multivariable analysis and to avoid redundancies with table 2, the univariate table is not included in the manuscript.

Discussion:

• “The overall mean of HRQOL among study participants was low and half of the respondents scored below the mean.” This statement appears recursive. The reader may expect that ½ of the subjects would score below the mean value in a normal distribution. A low score means little without comparison to a control group or a comparison of adjusted QOLIE scores between studies.

Response: “Half of the respondents scored below the mean”. This expression of result is now mitted. “The overall mean of HRQOL among study participants was low” is restated as “The overall mean of HRQOL among study participants was low compared to other scores in Ethiopia and the global mean score.” Thank you for the comment.

• A strength of this study is the diversity of citations to other studies. The authors, in the second paragraph, bring out these comparisons with a variety of other samples. I recommend at least summarizing these findings in the Introduction to allow the implicit comparison made in the Discussion opening sentence. Is there a citation or several that sets the precedent for comparing adjusted scores across studies? Please cite them.

Response: thankfully we organized those findings under the introduction section that were used for comparison in the discussion section of this revision. Citations used for comparing adjusted scores were all cited.

• The authors note that “being illiterate” was inversely…” This raises the need to specify who and how surveys were obtained in this study.

Response: this is restated as “being illiterate was negatively affecting overall HRQOL”, so illiteracy can result in low HRQOL in epilepsy score and worsen QOL of adult epileptic patients.

Thank you once again for your time and professional contribution.

Response to reviewer #2:

We want to thank you for your constructive comments. We incorporated almost all the comments provided in the manuscript as much as possible.

- The authors state throughout that the HRQOL was low at 55.6. In the discussion, they state "low when compared with other findings." It would be helpful to be more specific - compared to what (healthy population, epilepsy patients in other countries? Patients with other chronic diseases?) According to the QOLIE-31 scale, I believe that 50 is a T-score representing the mean HRQOL for a group of patients with epilepsy. In addition, the authors report that half of the patients scored below the mean. Is this not expected? I would appreciate a bit more information to better understand the interpretation of their findings.

Response: More information was added to the interpretation of the QOLIE-31 score of our study and discussed concerning the conclusion that it is low compared to other findings of QOLIE-31 scores in Ethiopia and other countries like the United Kingdom and Malaysia and also compared to the global...
mean score. So, we restated the interpretation sentence in the discussion section as "According to this finding, the overall mean of health-related QOLIE-31 among study participants was low (55.6) when compared with other findings of QOLIE-31 and the global mean score (59.8)". So the comparison was made with a similar population and similar tool (QOLIE-31).

- The discussion of HRQOL across the world could be more complete (for example, see Altaf Saadi et al., Quality of life in epilepsy—31 inventory (QOLIE-31) scores: A global comparison. Epilepsy & Behavior 2016 65:13-17.

Response: Thank you for your comment. We found Altaf Saadi, et al. is the best suggestion that we picked the global mean score of QOLIE-31 and used in discussion.

- Overall, it seems surprising that the variables identified could be independent. In fact, throughout the discussion, possible relationships between these variables are hypothesized, and I believe that these may be of significant interest (for example, factors associated with increased stigma, and effects of increased social support on other variables). Per the methods, the authors checked for multicollinearity and interaction terms between several of the variables and did not find any significant issues. Could the authors please help me understand how they chose which interaction terms to look at and the relevance of some of these factors possibly being associated?

o Might these possible interactions impact or simplify the conclusions if associated covariates could be grouped?

o If there are no such associations, then I would suggest editing the discussion to identify reasons that might be independent or other factors that might underlie the identified associations.

Response: The associated variables were reported as independently associated with HRQOL in epilepsy. “Independent” is used to signify that in the multivariable model, all variables which could be potential confounders were adjusted in the final model. So this is to mean a factor is associated with HRQOL independent of the effect of a confounder variable. Moreover, the built model is free of the effect of multicollinearity and interaction. The interaction terms created were "seizure frequency with depression, seizure frequency with stigma, seizure frequency with anxiety, seizure frequency with self-esteem, anxiety with depression and depression with self-esteem and they were all not significant”. So the identified variables were independent and the relationship between HRQOL and the associated factors would not be changed depending on other combined exposure variables. As we tested the effect of several variables on a single outcome variable (HRQOL), we tested whether the association of the identified factors with the outcome variable were free or independent of the effect of the interaction. Therefore, we edited the discussion as you suggested for the reasons that might be independent as the analysis has no other factors that underlie the identified associations. Thank you for your outlook.

Thank you once again for your time and professional contribution.

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**VERSION 2 – REVIEW**

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<th>REVIEWER</th>
<th>Quigg, Mark</th>
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</thead>
<tbody>
<tr>
<td>University of Virginia, Neuro</td>
<td>06-Nov-2023</td>
</tr>
</tbody>
</table>

**GENERAL COMMENTS**

The authors successfully addressed most of the major organizational issues, citation deficiencies, and omissions of the first version. Remaining issues fall mainly in the realm of editing: ESL, redundancies, and overall length.

1. Abstract: Please add to “Main outcome measure: Health-related quality of life in epilepsy measured using QOLIE-31 health survey” [evaluated as a dependent variable with simple and multivariable linear regressions].
2. Methods/Data Collection Procedure: The section “The QOLIE-31 was used…overall health [25].” belongs in the earlier section “Outcome Variable”.

3. Introduction/Discussion: the new version provides comparable data from different countries much more clearly than before. I strongly suggest that the paper would benefit by collecting the QOLIE 31 scores from other countries into a Table and ranking them by QOLIE score. Editing heavily the text where these listings lie could then be accomplished. That would save text and enable the synthesis of their findings in context rather than the authors’ current almanac-style listings of scores. For example, rather than the unremarkable overall conclusion that QOLIE scores “are low”, the authors could also state that the patients from Ethiopia rank in the xx quartile of regions evaluated in comparable studies. Also, since many don’t know what “low” means, in Methods in the QOLIE / main outcome section one could state what the range and median scores are for QOLIE31.

4. Discussion/page 12 lines 43 and page 11 lines 43. Seizure frequency as an influence on QOLIE is discussed twice. I recommend consolidating.

5. Discussion/limitations: the authors should mention that the multiple influences on QOLIE are likely not truly independent.

REVIEWER
Inati , Sara K
National Institutes of Health, NINDS

REVIEW RETURNED
21-Nov-2023

GENERAL COMMENTS
Thank you. I believe most of my comments have been adequately addressed. The one remaining scientific concern is a lack of clarity in the text as to exactly how this study was carried out. The response to the question of reviewer 1 actually made this less clear to me. It is stated that the study was carried out from March 25-May 6, 2019. 346 patients were included based on the power analysis in what is described as random sampling, with 6 subsequently excluded. Were the questionnaires administered to all 698 patients and then these were retrospectively selected? Or was the sampling prospective and questionnaires only administered to the 346 included patients? The response states retrospective random sampling. If so, how many patients were given the questionnaires? And as the reviewer stated, why not use all of them?

Remaining minor comments for improved clarity:
- The authors added a strengths and limitations of this study section to the abstract. Is this required? These points are currently quite awkwardly worded. For example, in point #2, better statistical analysis compared to what? The last two limitations seem better suited for the discussion.

Intro:
- In the first sentence, seizures do not always involve involuntary movements. Please re-word using standard definitions of seizures.
- Consider re-wording the 2nd sentence: “It remains a highly prevalent and often neglected major cause of disability….”
- Consider re-working the 1st sentence in paragraph 3: “There is a large literature assessing epilepsy quality-of-life using the QOLIE-31 inventory. The mean score across the globe is 59.8, ranging in specific cities and countries from….”
The sentence "mean quality of life of people living with epilepsy …" describing a study in Ethiopia appears to belong in the next paragraph.

Methods:
- Study setting and period: consider changing “currently” to “at the time of this study, the clinic was providing service to approximately 736 adult patients with epilepsy.”
- Sample size and sampling procedure: for the first sentence, consider “Based on a previous similar study conducted in Ethiopia, we assumed a standard deviation of the…”
- Data Collection: consider changing to just Data Collection Procedures. The previous section just described all of the instruments. And consider shifting the included information about the QOLIE-31 to the previous section where it was introduced (outcome variable).

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**VERSION 2 – AUTHOR RESPONSE**

Response to reviewer #1:
Thank you for your helpful comments. All comments were addressed in the revised text. Editing issues regarding ESL and redundancies were also resolved.

1. Abstract: “evaluated as a dependent variable with simple and multivariable linear regressions” is added to the main outcome measure and finally stated as “Health-related quality of life in epilepsy measured using QOLIE-31 health survey evaluated as a dependent variable with simple and multivariable linear regressions”.

2. Methods/Data Collection Procedure: your comment to the section “The QOLIE-31 was used….overall health [25].” belongs in the earlier section “Outcome Variable”. This redundancy regarding the measurement tool was solved by removing it from the data collection procedure and elaborating it only under the outcome variable measurement. Thank you for the comment.

3. Introduction/Discussion: thank you for the comment, as per your comment QOLIE-31 scores from other countries were tried to be listed in rank, but we could not find the national QOLIE-31 score of Ethiopia to indicate it in xx quartiles compared with other nations and sub-national scores were merely indicated for this reason. Also in the methods section, under the outcome variable, the cutoff of > 50 for the total scores each patient should score to be declared as leading a better life is indicated as per Vickery’s manual. Accordingly, the conclusion was also edited as “Only half of the epileptic patients in the study area are leading better quality of life and the overall mean health-related quality of life score is lower compared to another score in Ethiopia and the global mean score”.

4. “Discussion/page 12 lines 43 and page 11 lines 43. Seizure frequency as an influence on QOLIE is discussed twice. I recommend consolidating.” This redundancy was edited in this revision.

5. “Discussion-limitations: the authors should mention that the multiple influences on QOLIE are likely not truly independent.” Thankfully this was added to the limitations section.

Response to reviewer #2:
We want to thank you for your positive comments. We as much as possible tried to incorporate all the comments provided in this revision.

- Our study design is cross-sectional and there was no prospective or retrospective follow-up conducted. The sample 346 was selected from the total patients at the psychiatry clinic registry book (sampling frame) of the hospital using simple random sampling by select case method in SPSS. This is why we stated random case selection was conducted and the term retrospective is used to indicate the information collected is historical as stated under the data collection section like “The information
was collected all through a retrospective patient’s clinical, psychological and personal history”. We did not recruit new patients but selected among the pool of patients already on follow-up in the clinic in our study, so patients are sampled and information is collected about their past experiences like drug adherence. Concerning the study period (March 25-May 6, 2019), the expression retrospective random case selection to indicate historical study may result in a clarity problem and this was edited as we explained above. Questionnaires were only administered to the 346 included patients. Thank you for your comments.

Responses to other minor comments are as follows:
- “The authors added the strengths and limitations of this study section to the abstract. Is this required? These points are currently quite awkwardly worded. For example, in point #2, better statistical analysis compared to what? The last two limitations seem better suited for the discussion.”
  Response: the strengths and limitations of this study next to the abstract section are indicated due to the journal’s requirement of the formatting style. The better statistical analysis i.e. linear regression is stated as a strength for the sake of safeguarding the loss of information for continuous outcome variables, but not in comparison with other statistical methods. We have already discussed the last two limitations.

Introduction:
“In the first sentence, seizures do not always involve involuntary movements. Please re-word using standard definitions of seizures.”
Response: A standard definition of seizure was inserted in the first sentence. Thank you for your comment in shaping the writing of this manuscript.
Consider re-wording the 2nd sentence: “It remains a highly prevalent and often neglected major cause of disability….”
Response: this is now re-worded as “It continues to be the most common, neglected, and one of the major causes of disability in Ethiopia, where an estimated 1 million people have epilepsy, of which 500,000 have active epilepsy (having experienced seizures within the last one to two years), and only 5% seek medical attention”.
Consider re-working the 1st sentence in paragraph 3: “There is a large literature assessing epilepsy quality-of-life using the QOLIE-31 inventory. The mean score across the globe is 59.8, ranging in specific cities and countries from…”
Response: the 1st sentence in paragraph 3 is restated as per your suggestion “There is a large literature assessing quality-of-life in epilepsy using the QOLIE-31 inventory. The mean score across the globe is 59.8, ranging in specific cities and countries from 42.1 in the Russian Federation to 82.0 in Canada [6]. Thank you for that.
“The sentence “mean the quality of life of people living with epilepsy …” describing a study in Ethiopia appears to belong in the next paragraph.”
Response: this was edited as you suggested. Thank you.

Methods:
“Study setting and period: consider changing “currently” to “at the time of this study, the clinic was providing service to approximately 736 adult patients with epilepsy.”
Response: Thank you for your feedback. I have incorporated your suggestions in this revised version.
Sample size and sampling procedure: for the first sentence, consider “Based on a previous similar study conducted in Ethiopia, we assumed a standard deviation of the…”
Response: thank you, this first sentence is re-written in this revision as “Based on a previous similar study conducted in Ethiopia [12], we assumed a standard deviation for the overall quality of life among patients with epilepsy of 20, and the margin of error decided to be 1.5 at a 95% confidence level.”
“Data Collection: consider changing to just Data Collection Procedures. The previous section just described all of the instruments. And consider shifting the included information about the QOLIE-31 to the previous section where it was introduced (outcome variable).”
Response: the title “Data Collection Procedure and Instruments” was changed to “Data Collection
Procedure” and descriptions of the instruments as well as information about the QOLIE-31 were transferred to the “Measurement of Outcome Variable and Exposure Variables” sections. Thank you for all your comments that improved this revised version of our manuscript.

VERSION 3 – REVIEW

**REVIEWER**  Quigg, Mark
University of Virginia, Neuro

**REVIEW RETURNED**  04-Dec-2023

**GENERAL COMMENTS**

The authors have improved the manuscript. I still don’t understand why they felt compelled to diminish their sample with a random selection scheme, but it seems benign enough. The style remains a problem, with redundancies or partial explanations that would benefit from consolidation. But, these style issues lie in the journal’s editor’s domain. I provide some specific observations that are editorial and suggested for clarity and brevity to illustrate changes that could be done in other parts. I do not need to review the revision.

1. Introduction:
- Suggest removing the first 2 sentences and start the 3rd as “Epilepsy has serious physical...”. The target audience knows what epilepsy is.
- The authors should consolidate the explanation of the QOLIE-31 in page 2 lines 10-12 to the start of the third paragraph page 1 lines 38-39.
- Change “The mean score across the globe is 59.8...” to “The mean global QOLIE-31 score is 59.8 (score range favorable xxxhighest possible – poor yyylowest possible), ranking from Canada (82.0), Uganda (58.0), ....”.
- Change “epileptic patients” to “patients with epilepsy (PWE)” throughout

Discussion
- first paragraph: please be specific in summarizing results. Make sure statements indicate the variable and the test source. Example: “The overall weighted mean score of HRQOL among study participants was low compared to another score in Ethiopia and the global mean score. The highest mean score was the medication effects and the lowest was the seizure worry domain.” Suggest “Patients in Ethiopia reported a mean QOLIE-31 score below the global median. The best QOLIE-31 subscale results were seen in medication effects, and the worst subscale results lay in the seizure worry domain.”
- Similarly: “Monthly income of >1000 birr per month, social support and being free of seizures for a year were positively affecting the health-related quality of life of adult epileptic patients. However, age, anxiety, depression, low self-esteem, perceived stigma, taking medication twice or more times per day, being illiterate and having more than two seizures for a year were negatively affecting adult epileptic patients' health-related quality of life.” Suggest “Factors such as greater income, greater social support, and seizure remission > 1 year were associated with better QOLIE-31 scores, whereas ....”

**REVIEWER**  Inati, Sara K
National Institutes of Health, NINDS
Response to reviewer #1:
Thank you for your helpful comments. All comments were addressed in the revised text. Editing issues were also resolved.
Random selection of cases was done not to diminish the sample but to adhere to a scientific way of giving every member of the study population an equal chance of being included in the study. The only thing impeding the study’s conduct among all epileptic patients on follow-up is a lack of resources.
The style of the manuscript is done to stick to the journal’s formatting requirements. As per your suggestion, certain redundancies were consolidated in this revision. We present other responses to the specific sections as follows.
1. Introduction:
- The introduction section starts with the third sentence as you suggested “Epilepsy has serious physical ….” Thank you for the comment.
- QOLIE-31 explanations on page 2 lines 10-12 were consolidated to the start of the third paragraph page 1 lines 38-39.
- The expression “mean score across the globe is 59.8…” was changed to “The mean global QOLIE-31 score is 59.8 (score range 82.0 – 42.1), ranking from Canada (82.0), Uganda (58.0), Warsaw (55.2), China (53.9), Bhutan (48.9) and Moscow (42.1) [5-10]”. Thank you for the comment, this saves words and at the same time is an informative expression.
- The expression, “epileptic patients” was changed to “patients with epilepsy (PWE)” throughout the manuscript.
2. Discussion:
- The first paragraph was revised as per your suggestions just to be more specific and informative in summarizing results.
We appreciate your valuable input, time, and expertise in helping to improve the scientific rigor of our article.
Response to reviewer #2:
We would like to express our gratitude for all of your expert input during the first and second reviews, which helped to strengthen the scientific quality of our manuscript.