

Peer-Review comments and author responses

Reviewer 1:

General Comment:

Dear authors, I congratulate you on the excellent article and the proposed analysis. The association between dietary factors and mental disorders is becoming increasingly evident, and your work greatly contributes to the literature on this topic. I have a few questions, comments, and suggestions.

1. Abstract:

-Comment: Perhaps the background section could be shortened to allow more space for the methods description and presentation of results. I believe it would be very important to include some information in the methods section, such as the definition of exposure (total, soluble, or insoluble fiber? Fiber from diet, supplementation, or both? Reported in grams per day and quartiles?), as well as the outcome (questionnaire for identifying depression and its severity? Medical records? Self-reported prior diagnosis?). Additionally, it would be useful to present the effect measure and confidence interval for the main exposure, complementing the sentence with the variables included in the adjusted model without going into too many details (just as an example: “Individuals consuming >30g/day of fiber had a lower chance of depression [OR 0.85, 95% CI 0.10 – 0.95, $p < 0.001$], independent of age, sex, poverty level, obesity...”). Given the limited space in the abstract, this will be the reader's first contact with your work.

Response: *Thank you for your suggestion. The abstract was rewritten including more information in the methods and results sections. Specifically, the abstract was rewritten to “Individuals were considered to be fiber supplemented if they reported consuming more than zero grams of fiber supplementation per day and depression status was assessed using the Patient Health Questionnaire-9 (PHQ-9), which a score above 9 indicates moderate to severe depression, which served as the cut-off point for this study. The model showed that individuals taking fiber supplementation had a lower chance of depression [OR, 0.75; 95% CI, 0.59 – 0.96, $p = 0.02$]”.*

-Comment: The introduction is well-structured and clearly presents the gaps in the literature that the study aims to address. My only suggestion is to ensure consistency throughout the text regarding the term "gender," which should be replaced by "sex" (I believe the variable collected in NHANES refers to biological sex, rather than gender identity). Additionally, I think the sentence "A multivariate logistic regression model was..." could be omitted here. One comment for the authors to consider: since this is a cross-sectional analysis, the term "a protective factor against..." may not be the most appropriate, as it is not a cohort study

where prognostic factors are more easily identified (perhaps replacing it with "negative association" would be more fitting?).

Response: *Thank you for your comments. Regarding the use of the “gender” term, it was referred to in this way in the NHANES spreadsheet, but the only options are “male” or “female”, hence we have changed it to sex. Additionally, the sentence “multivariate logistic regression model was...” was removed and the sentence “protective factor...” was adapted according to your suggestion.*

-Comment: It is important to indicate the meaning of the abbreviations used in the figure legends (for example: PHQ9, BMI). Regarding abbreviations, I suggest reviewing the document, as the description of some abbreviations appears later in the text rather than at their first mention.

Response: *Dear reviewer, we appreciate your input. We have corrected the abbreviations on a first-mentioned instance basis for a more comprehensive reading and added the label in figure 1..*

-Comment: What was the rationale behind the authors' decision to dichotomize fiber supplementation into "zero" and "more than zero grams/24 h" in the dichotomous analysis? It would be important for the authors to explain this rationale or include a reference to other studies that have used the same approach.

Response: Thank you very much for your consideration. We dichotomized fiber supplementation into absence of fiber supplementation (about 60% of individuals in the NHANES 2017-2018 database), and any amount of fiber supplementation. The following text is present in our corrected version of the manuscript: “Therefore, this variable was transformed from continuous to dichotomous, considering individuals as supplemented if they reported more than zero grams/24 h of fiber supplementation in their diet”.

-Comment: Still regarding the exposure: if the variable related to fiber intake from food is not available in the database, and only information on fiber supplementation is provided, this should be clearly stated both in the introduction and in the methods section. This is important because most studies assess not only supplementation but total fiber intake — from both food and supplements. Additionally, this point needs to be discussed, as many fiber-rich foods contain other nutrients within their matrices that are also associated with a lower likelihood of mental disorders. This could be a limitation, as the lack of this information in the database represents a significant confounding factor that was not considered in the model (for example, an individual might have a poor diet overall but only use a fiber supplement; this does not guarantee they have a high-quality diet, which is associated with a decreased likelihood of depression [a small example: <https://pubmed.ncbi.nlm.nih.gov/39477074/>]).

Response: Thank you for highlighting the importance of defining the exposure, we modified the introduction section and described the methods section regarding fiber supplementation, instead of fiber intake. Additionally, we stated as a limitation that since fiber intake was not considered, further longitudinal studies are needed to assess the impact of daily consumption in the development of depressive symptoms.

-Comment: Which covariates were assessed? The authors mention that "comorbidities were categorized as 'yes' or 'no' for at least one comorbidity," but they do not specify which comorbidities were considered.

Response: Dear reviewer, thank you for your question. In NHANES 2017-2018 dataset, the variable does not specify any specific comorbidities. It only mentions "at least one comorbidity".

-Comment: In the statistical analysis section, I suggest revising the sentence "A univariate logistic regression model was built to determine the impact of fiber supplementation in the development of depression symptoms." The terms "impact" and "development" suggest a longitudinal analysis, particularly one involving an intervention.

Response: Thank you for your comment. Agreed and the sentence was rewritten: "A univariable logistic regression model was built to determine the relationship of fiber supplementation with depression symptoms."

-Comment: Regarding Table 1: In general, in cross-sectional analyses, groups are compared according to the exposures (please refer to this other study with NHANES data as an example: <https://pmc.ncbi.nlm.nih.gov/articles/PMC9511583/>), rather than according to the presence of outcomes (this approach is more commonly seen in case-control studies). Is there any justification for this comparison in the analysis presented by the authors?

Response: Thank you for your suggestion, as this is a cross-sectional analysis we agree that the columns must be modified to represent the exposure. We hope the new table 1 reflects this change, and we appreciate this review as it has improved the manuscript.

-Comment: My suggestion for Table 2 is to also present the reference categories. For example: "Ever told you had a thyroid problem?"; it is not clear whether the OR presented is for "yes" or "no." A possible way to present this could be:

Thyroid problems	
No	1
Yes	1.375 (1.003 – 1.886)

Response: Thank you for your suggestion. Table 2 was changed accordingly.

-Comment: I would suggest presenting the secondary analysis first, followed by the sensitivity analysis.

Response: *Thank you for your comment. We agree and the order of the secondary analysis and sensitivity analysis sections was changed.*

-Comment: Since the authors mentioned the role of the microbiota as a potential mediator between fiber intake and depression, it might be interesting in the discussion to briefly describe the potential mechanisms involved in this relationship. For example, could short-chain fatty acids, metabolites produced by the microbiota, stimulate or inhibit any markers produced at the intestinal level, such as serotonin? This could help further clarify the biological pathways underlying the observed association.

Response: *Thank you for this insightful suggestion. We agree that discussing the potential mechanisms through which the microbiota may mediate the relationship between fiber intake and depression would provide valuable context for the reader. We addressed this topic in the second paragraph of the introduction.*

Reviewer 2:

-Comment: Thank you for such nice and excellent job, here is my feedback and suggestions;

1. Title:

-Comment: It does not represent and match the primary objective; I suggest to concise and match the primary objective.

Response: *Dear reviewer, thank you for your recommendation. We have delimited the title as follows: "Association between fiber supplementation and depression in US adults: Data from National Health and Nutrition Examination Survey (NHANES) 2017–2018."*

2. Abstract:

-Comment: I recommend to be written in more academic Format.

Response: *As suggested, the abstract has been modified to a different and more precise academic format.*

3. Introduction:

-Comment: Elaborate more regarding Knowledge gap, why Previous studies are still controversial/not conclusive (give elaborations and examples).

Response: Dear reviewer, previous research has been done addressing how fiber supplementation decreases the prevalence of depressive symptoms as we have found in the literature; yet, the role of fiber remains inconsistent since a large number of covariates are not accounted for when investigating this relationship.

-Comment: What about the secondary objectives?

Response: Thank you for your comment, we acknowledge that the secondary objective was not added to the introduction. Therefore this statement at the end of the study was added “ In addition, a multivariable logistic regression was made to evaluate the association between the quantity of fiber supplementation and moderate to severe depression, as a secondary objective”.

-Comment: Methods: - Duration format at least month/year e.g. Jan 2017 to Dec 2018

Response: Thank you for your concern about the format of the duration in the methodology section. We revised the NHANES website for the 2017-2018 entry and could not find any further specifications for the duration of the data collection.

-Comment: State Clearly the primary outcome

Response: Thank you for your suggestion, the outcome section has been revised to clarify the variables for our primary outcome.

-Comment: List eligibility criteria

Response: We appreciate your recommendation and we have decided to add an eligibility criteria section specifying this information.

-Comment: What is the validity for your covariates' categories?

Response: The covariates are detailed in the “Covariates” section. We categorized the variables according to the information in the NHANES dataset.

-Comment: I advise to create flow chart for this section.

Response: The Figure 1 displays the participants selection in a flow diagram.

4. Result:

-Comment: I advise to divide it into descriptive and inferential, in order following your objectives.

Response: We appreciate your concern about the organization of our results. We have decided to create 2 subcategories for “Population description” and “Explanatory analysis”.

5. **Discussion:** in this session you need to elaborate more about the rationale of your findings and if they are similar or difference from literature review. In addition, you need to admit the study limitations and your recommendations.

Response: Thank you for your input on our discussion section. We have expanded on the meta-analysis results for the association between fiber intake and risk of depression.

-Comment: References: use same format and try to avoid references older than 20 years.

Response: Thank you. All references have been checked and the time length addressed as recommended.

Reviewer 3:

-Comment: Based on the content, minor revisions are recommended. The paper has significant strengths, and addressing the outlined areas will enhance its clarity and impact while aligning with the journal's focus on advancing science.

1. Strengths of the Study

- The study addresses a relevant topic: the association between fiber intake and depression, which has potential public health implications.
- Use of a large, representative sample from NHANES enhances generalizability.
- Comprehensive adjustment for covariates provides a more nuanced understanding of the relationship between fiber and depression.
- The use of standardized measures (PHQ-9) and validated statistical approaches strengthens the reliability of the findings.

2. General Recommendations

-Comment: Clarity and Flow: The paper is well-organized, but some sections could benefit from minor rephrasing to improve clarity (e.g., the abstract's first sentence could be streamlined).

Response: Thank you for your comments and suggestions for the improvement of our manuscript, we have carefully reviewed the manuscript and made the changes necessary for clarity improvement.

-Comment: Consistency: Ensure consistent terminology throughout the paper, such as referring to fiber supplementation as "supplementary fiber intake" in all sections.

***Response:** Thank you for noticing this inconsistency in our manuscript. We revised it to ensure that fiber supplementation substitutes for fiber intake wherever necessary.*

3. Addressing Limitations

-Comment: - Acknowledgement of Limitations: While the discussion addresses the lack of ICD-10 codes and self-reported data, it should further emphasize the implications of these limitations on interpreting the findings.

***Response:** Dear reviewer, thank you for your suggestion on highlighting the importance of how self-reported data can be a source of bias. We modified the text accordingly.*

-Comment: The cross-sectional design limits causal inferences. Suggest explicitly recommending longitudinal studies to better establish temporal relationships.

***Response:** Thank you for highlighting the limitations of cross-sectional studies. We have included recommendations on longitudinal studies to assess causality and temporal relationships between fiber supplementation and depressive symptoms.*

4. Suggestions for Improvement:

-Comment: Clarify the limitations of fiber supplementation versus dietary fiber intake from food. Consider discussing how this distinction might impact the generalizability of the findings.

***Response:.** Thank you for your suggestion. In order to avoid inconsistency, we modified in the manuscript changing fiber intake to fiber supplementation.*

5. Discussion and Conclusions

-Comment: Conclusions Alignment: The conclusions are well-supported by the results, but they should be framed more cautiously given the limitations. For instance, emphasize the need for further studies to confirm causality.

***Response:.** Thank you for your comment, we changed the scope of the conclusion to comply with your nice suggestion.*

-Comment: Expand on the implications of poverty and comorbidities, especially since these factors showed stronger associations than fiber supplementation in the multivariate model.

***Response:.** We appreciate your feedback, and we included some of the implications in comorbidities.*

6. Future Research:

-Comment: Encourage exploration of specific sources of fiber and their potential differential effects on mental health.

Response: Thank you for your suggestion. We add the following sentence to the discussion section: “It should be noted that different fibers may differ in their efficacy, suggesting a future research line.”

-Comment: Suggest investigating how combinations of protective factors (e.g., fiber intake, physical activity, and social relationships) interact to influence depression risk.

Response: Thank you for your suggestion, we added to our conclusion the statement for suggesting further research on protective factors.