Dear Editor,

We wish to express our sincere appreciation for the valuable feedback and constructive comments provided by you and the distinguished review panel regarding our manuscript entitled “Association between composite dietary antioxidant index and stroke among U.S. adults with diabetes—Insights from NHANES” (Manuscript ID: 94414).

In response to the insightful comments received, we have meticulously reviewed and revised our manuscript. Detailed, point-by-point responses to the reviewers’ comments are presented below. To facilitate the review process, all changes made in the manuscript are highlighted for easy identification and comparison.

I would like to declare on behalf of my co-authors that the work is original research and has not been published previously or under consideration for publication elsewhere, except that this study will be presented at the 84th American Diabetes Association (ADA) Scientific Sessions/Annual Meeting in Orlando, June 21-24, as oral presentation.

We look forward to hearing from you soon regarding our submission.

Yours sincerely,

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Reviewer #1:

The study in this manuscript is interesting. However, it should be edited to improve presentation and originality. Several previous works have reported CDAI-Stroke relationship, including some in your bibliography such as "Wang T, Liu H, Wei X: Association between the Composite Dietary Antioxidant Index and Stroke: A cross-sectional Study. Biological Trace Element Research 2023." Then, edit to highlight the novelty and singular aspects (the population, the findings). In discussion increases comparison with previous works, further you can include some quantitative analysis compared with reported values. The conclusions section should include the aspects and variables which let you to support the inverse relationship in the first sentence. But relevant, the second sentence is confusing. How your results underscore the potential of a diet rich in diverse antioxidants in reducing stroke risk...? I guess you Must edit that to be clear in the meaning regarding your work and those previously reported.

Response: Thank you for your thoughtful feedback and for acknowledging the interest of our study. We appreciate your suggestions on how to enhance the presentation, originality, and clarity of our findings. In response to your comments, we have undertaken a thorough revision of our manuscript with a focus on improving these aspects:

1. Highlighting Novelty and Uniqueness: We have revised the introduction and discussion sections to better highlight the novel aspects of our study. Specifically, we emphasize the unique characteristics of our population sample, which focuses on individuals with diabetes, differing significantly in demographics and dietary habits from those in previous studies. Furthermore, we highlighted the originality of our findings, as we are the first to demonstrate the significant role of the Composite Dietary Antioxidant Index (CDAI) in reducing stroke risk in this high-risk group. Additionally, through the use of restricted cubic splines, we observed
that as CDAI increased, the risk of stroke gradually decreased. These modifications aim to better showcase the unique contributions and innovative aspects of our study.

2. Enhanced Comparison with Previous Works: We have expanded the discussion to include a more detailed comparison with earlier studies. This includes a quantitative analysis where our results are directly compared to the reported values in the literature, highlighting both consistencies and discrepancies. This comparative analysis further underscores the contribution of our study to the field.

3. Clarification of Conclusions: We have made the requested modifications and adjustments to more clearly convey the significance of our research findings. We hope these changes meet your expectations and that you are satisfied with the revisions. Here is the revised conclusion section:

In summary, this cross-sectional study found that adults with diabetes in the United States with high levels of the CDAI, which measures the overall antioxidant quality of the diet, tend to have a lower risk of stroke. Furthermore, our smooth curve fitting analysis revealed a negative relationship between CDAI and stroke. Based on these findings, it is recommended that patients with diabetes maintain an appropriate intake of dietary antioxidants to increase their CDAI, thereby reducing stroke-related risk factors. In the future, high-quality prospective studies are needed to confirm our results and provide further insights.

With these revisions, we have clarified the inverse relationship between CDAI and stroke risk and provided practical recommendations based on our findings. Additionally, by supplementing the conclusion with more detailed descriptions and modifying the wording, we have supported the inverse relationship and eliminated any ambiguity.

We hope these revisions address your concerns and enhance the manuscript by clearly delineating its original contributions and strengthening the presentation of our results. Thank you once again for your valuable insights, which have been instrumental in refining our paper.
Reviewer #2:
Dear Authors I find the content and the concept very good keeping in view of the dietary influence on the diabetes directly and to stroke indirectly. I would like to mention whether 24 Hr dietary status could give overall account of the dietary status of the patient and could we accurately estimate the CDAI. May I get a descriptive explanation for that.

Response: Thank you for your encouraging remarks on our manuscript and for your insightful query regarding the use of 24-hour dietary recall to estimate the CDAI. We appreciate your interest in the methodological aspects of our study. To address your inquiries and clarify any confusion, we would like to provide a detailed explanation. Dietary information was obtained from dietary interview which was conducted in the NHANES Mobile Examination Centers (MECs). The dietary intake data are used to estimate the types and amounts of foods and beverages consumed during the 24-h period prior to the interview, and to estimate intakes of energy, nutrients, and other food components from those foods and beverages. This method involves participants recalling their diet from the previous day, thereby minimizing memory-related errors, and it involves a comprehensive analysis of dietary intake data to quantify the intake of various antioxidants. Trained professionals conduct these interviews using standardized methods to ensure data quality. Standardizing the intake of each antioxidant in the calculation of the CDAI helps to reduce errors caused by individual dietary variations. By converting antioxidant intake into standardized scores (z-scores), the data becomes more consistent and comparable across different individuals. This reduces bias from varying dietary habits, leading to a more accurate and reliable measure of the CDAI. While the 24-hour dietary recall is an extensively validated tool used in nutritional research, we acknowledge in the limitations section of our discussion that this method may not capture day-to-day variations in individual dietary patterns. However, its widespread validation in large-scale studies, including NHANES, supports its utility in estimating average dietary intake across diverse populations. By clarifying this in both the methods and limitations sections, we aim to provide a balanced view of the strengths and limitations of our methodological
approach, enhancing the manuscript's rigor and transparency. We hope this addresses your concerns and illustrates the robustness of our methodology. Thank you once again for your valuable comments, which have significantly contributed to the precision and depth of our manuscript.

Reviewer #3:
The authors highlight the significance of dietary antioxidants in stroke prevention, which presents an intriguing finding. They have examined the relationship between CDAI and stroke, advocating for the utility of antioxidants in the prevention of stroke. The quality of this manuscript is good, and the conclusion appropriately summarizes the data provided by this study. It also touches upon the mechanisms of how each antioxidant mitigates cellular damage, with ample discussion provided. This publication is likely to have a significant impact on future research from the perspective of stroke prevention. However, there are several issues that need to be addressed, as outlined below.

1. The authors said that stroke is the fourth leading cause of death worldwide in the introduction part, but according to the latest data of WHO research, it is the second leading cause of death worldwide. ([https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death](https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death))

   **Response:** Thank you for your careful reading of our manuscript and for pointing out the discrepancy regarding the ranking of stroke as a cause of death worldwide. We appreciate your attention to detail and the opportunity to correct our manuscript to reflect the most current data. In response to your comment, we have updated the introduction of our manuscript to accurately represent stroke as the second leading cause of death worldwide. We have provided the updated reference to ensure the accuracy and reliability of our manuscript. We believe this correction enhances the manuscript by providing a more accurate context for the significance of stroke prevention and further underscores the importance of our findings regarding dietary antioxidants. Thank you for helping us improve the
quality and accuracy of our work.

2. The authors should not only mention the full term for CDAI in the abstract but also provide the full form of the abbreviation the first time it is used in the main text.

Response: Thank you for your constructive feedback regarding the use of abbreviations in our manuscript, specifically the term CDAI (composite dietary antioxidant index). We understand the importance of clarity for all readers, especially those who may not be familiar with this specific term. In response to your comment, we have revised our manuscript to include the full term "composite dietary antioxidant index (CDAI)" upon its first mention in both the abstract and the main text. We have ensured that the abbreviation, CDAI, is consistently introduced after the full term throughout the document to maintain clarity and readability. We appreciate your guidance in enhancing the accessibility and professionalism of our manuscript.

3. In the introduction part, the authors said "Unlike single antioxidants, the CDAI offers a more comprehensive assessment of overall antioxidant intake, correlating with oxidative stress and inflammation biomarkers.". They should include references for the content mentioned.

Response: Thank you for highlighting the necessity to substantiate our claims with appropriate references, your insight is invaluable in enhancing the credibility and scholarly depth of our manuscript. According to your instruction, we have added relevant references and details in the introduction part to substantiate this claim and provide a robust background for our study's methodology. We hope these changes satisfactorily address your concerns and strengthen the manuscript. Thank you once again for your constructive comments.
Thank you for your valuable feedback on our manuscript. Your comments are crucial for improving the quality of our paper. We have carefully reviewed and addressed your suggestions, making the necessary enhancements and optimizing the details of the article. Below are the modifications we have made: First, we have detailed the calculation process of the CDAI, dividing it into three steps and specifying the calculations for each step. We believe that this addition makes the calculation process of the index in the article clearer. Additionally, we have included the corresponding calculation formulas to facilitate a more intuitive understanding of the process. Thank you again for your suggestions and guidance. If you have any further suggestions or need more information, please feel free to contact us. We look forward to receiving your feedback on our revised manuscript soon.

Yours sincerely, Chaofan Wang, MD, Associate Chief Physician Department of Endocrinology and Metabolism The Third Affiliated Hospital of Sun Yat-sen University Guangdong Provincial Key Laboratory of Diabetology Guangzhou, 510630, China Email: wangchf25@mail.sysu.edu.cn ORCID: 0000-0001-5292-5564