Peer-Review comments and authors responses

"Association Between Self-Reported Diabetic Diet and LDL Cholesterol Levels in U.S. Overweight and Obese Adults: A Cross-Sectional Analysis of NHANES 2017–2018"

Reviewer 1

Title

Comment 1: The title implies that LDL is related to obesity, which is not absolutely true. You can focus only on the cardiovascular risk.

Response: We changed the title to be more specific regarding our population and findings: "Impact of a Self-reported Diabetes-Focused Diet on LDL Cholesterol Levels in Overweight and Obese Adults."

Introduction

Comment 2: You mentioned why diabetic diet has been studied, but can you mention if there are other diets and whether studies compare them to diabetic diet?

Response: We added reference to Fathy A. et al., which compares three diet types and their metabolic effects in type 2 diabetes.

Methods

Comment 3: You mentioned exclusion criteria familial hypercholesterolemia, is it reported in NHANES? A sensitivity analysis could give you more robust results considering your null finding and small sample size.

Response: Familial hypercholesterolemia is not measured in NHANES; therefore, we included it as an exclusion criterion. A sensitivity analysis was not possible.

Results

Comment 4: Table 1 shows higher BMI in the diabetic diet group. Does diabetic diet lower BMI?

Response: We clarified in the Discussion that individuals reporting a diabetic diet tend to have higher BMI, likely reflecting an older subgroup with established diabetes.

Discussion

Comment 5: Discuss confidence intervals, not only significance.

Response: We revised the Discussion to address precision and interpret confidence intervals more explicitly.

Limitations

Comment 6: What was the diet duration or adherence quality? mention potential residual confounders. You can acknowledge the limitation of a cross-sectional study like this to evaluate if diet lowered LD or people who had high LDL started diet, or people started diet and statin simultaneously. This is a limitation of the study. Also, self-reported diet without validation (bias).

Response: We expanded the Limitations section to include lack of adherence data, self-reported diet, residual confounding, and the inability to infer causality.

Reviewer 2

Abstract

> **Comment 1:** The last sentence in the background is misleading. The relationship between diets and LDL is not unclear (Schoeneck et Iggman 1016/j.numecd.2020.12.032). This must be rewritten. Btw. You mentioned this yourself in the first sentence of the third paragraph in the intro. In the objective, it is also somewhat misleading as it tests the association between adherence to a diabetic diet. While I understand it is intended as the exposure variable "adherence to diet," it sounds more like you are actually investigating the adherence rate, which you are not.

Response: We modified the last sentence of the background text to create a more coherent narrative. In the methods section, we removed the term "adherence." We modified some aspects of the results and conclusion according to the suggested changes.

> **Comment 2:** I am missing the reference for the second sentence (dylipedemia,…). First sentence of the third paragraph: references. Then the following sentence, the "moreover […] lacks is misleading since the first sentence does not mention a lack in research at all.

Response: We added the reference for the second sentence which is (Abere et al, 2024). We modified the structure of paragraph 3 to make it more direct.

Methods:

> **Comment 3:** First of all, the paragraphs under "Methods" and those under "Database and study population" are redundant; they both kind of provide the whole method section. References do not list all authors correctly. - Your second paragraph names exclusion criteria, which is good, but why not mention the exclusion of other diets here instead of the third paragraph?While it is good that you mentioned the ethical consideration, those are not your ethical consideration (as thus you can't provide the ethical numbers for it). Better, you mentioned this is a survey with IRB-approved data, and since the data was provided anonymously and publicly, you don't need your own IRB.

Response: We improved the aspect that the survey was conducted with IRB-approved data. Regarding the description of diabetic diet, we found no information in NHANES database about standardized or operational definition of what constitutes a "diabetic diet." It was a participant's perception response. About the description of the sample, familiar history stands for history of diabetes and myocardial infarction. Metabolic conditions stand for presence of high blood pressure and dyslipidemia. About the difference size sample (2150 x 2042) after the adjusted analysis, we described in the discussion that it was not a mistake - develop better. .

Results:

> **Comment 4:** In general more active voice than passive voice. In the second and third paragraphs, you name changes to "older", "more common", "Slightly", which imply there is no significance, but there is! Name it, they are significantly older, statins are significantly more often in… Fourth paragraph: the LDL is not 18.6 (mean), there is a 18.6 difference between the two groups. Why the cut-off at 50 years of age for effect modification? It seems totally random. Since you have a significant difference for diabetes, why not a subgroup analysis? Moreover, by now it is not clear whether you have active diabetes or a history of diabetes, as this variable? In the mediation analysis, you mention the educational level, but never before or after it was mentioned again.

Response: We thank the reviewer for this comment. We have revised the Results section to report the statistical significance of key differences. Participants following a diabetic diet were significantly older

(62.53 vs 49.89 years, p < 0.001), statin use was significantly more frequent (38.46% vs 16.97%, p < 0.001), HbA1c was significantly higher (7.74% vs 5.78%, p < 0.001), and LDL-C was significantly lower (91.69 vs 110.29 mg/dL, p < 0.001). We replaced terms like "older," "more common," and "slightly" with language reflecting statistical significance.

We excluded the educational level, it .was not included in the baseline characteristics. The cut-off of 50 years was selected to create two groups of roughly comparable size for effect modification analyses. We acknowledge this is somewhat arbitrary, but sensitivity analyses using alternative age cut-offs (e.g., 55 or 60 years) yielded similar results.

We agree that diabetes status is an important potential effect modifier. However, given that over 90% of participants reporting a diabetic diet also had diabetes, the non-diabetic subgroup within this category was too small to yield reliable estimates. For this reason, a stratified (subgroup) analysis by diabetes status was not conducted. Instead, diabetes history was included as an adjustment variable in the multivariable model to control for its confounding effect.

In the present analysis, we included both participants with and without diabetes to ensure an adequate comparison group and broader representativeness of the NHANES population. However, we acknowledge that focusing specifically on individuals with active diabetes would provide a clearer understanding of dietary effects within this clinical group. This will be addressed in a subsequent analysis with a diabetes-focused approach.

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Discussion

Comment 5: In the first sentence, you mentioned overweight and obese patients, but you haven't restricted them in the analysis, as can be seen from your BMI table. So what have you actually analysed? The first two paragraphs are just results, this can be more comprehensive as it is nearly the same length as the results. This part focuses more on discussing your results in relation to existing literature.

Third paragraph: I don't need the title of a paper, mention what's in it and what's relevant for your discussion

Fourth paragraph, first sentence: I don't understand the rationale behind your statement here. When statin use is inefficient and thus leads to a smaller decrease in LDL, how would this reduced decrease based on statins influence your non-findings in the multiregression analysis? Shouldn't it be better for the effect of the diet on LDL?

Fourth paragraph, second sentence: Just because it is mentioned that LDL rises with BMI in thinner people doesn't mean it is not reduced by diet in all? What is the point here? You state something, but I am missing the context towards your research.

Fifth paragraph: You mention the collinearity for diabetes status and HbA1c. Why haven't you just tested it? Moreover, then you should include one of those variables in the regression analysis, not both.

Sixth paragraph: "This highlights for clinicians…": No. This is too judgmental based on your findings and the discussion you provided. With such a low number, you can't make such great assumptions. Again, you mentioned here obese people, but no data on them. In General: I am missing more content in other papers. For instance, you have diabetes as an effect modifier, and provide some reference for those with cardiovascular diseases, but not for the general population (like this MA from Neuenschander et al. /10.1007/s10654-019-00534-1). Or what could be the impact of age differences? I can imagine that older people are more focused on their diets, but their lower metabolism could affect the findings. (This is not generalizable)..

Response: The population is clarified in the methods and results part and addressed in the discussion. Improvements were made to discuss our results based on previous literature instead of just result repetition on the discussion, as well as clarification on the benefit of statins on LDL levels. Collinearity between HbA1c and diabetes presence were adequately tested and justified why both variables were considered. Age differences were addressed in the discussion as well as clarification for clinical significance of the results.

Tables

> **Comment 6:** I am not sure about what the comparison is for the gender here; is it within the males, but then why not a test in the females or is it within the exposure groups, but again, why just one stat?

Response: Thanks for the comment, we addressed this topic about the tables and update the information for more clarification about the population gender and the results in female.

Reviewer 3

Introduction

> **Comment 1:** The introduction: mentions that diets are recommended in cardiovascular prevention. Indeed, some diets are recommended to reduce cardiovascular risk, but their effect on LDL cholesterol is not established, which is not clear in your first paragraph, but becomes clearer in the third. Furthermore, when you mention recommendations, I would suggest citing guidelines, such as ACC/AHA and/or ESC guidelines. When introducing the diabetic diet, you explain that it is recommended, but I would suggest elaborating more about why it is recommended, i.e., which favorable effects are known (or not known, which can justify your study). Your third introduction paragraph about the need to disentangle the effect of diet from other contributions is an excellent justification for this study.

Response: We clarified that there are no current guidelines that suggest a specific diet but the American Diabetes Association recommends nutritional evaluation and lifestyle modifications. We deepened on when the diabetic diet is indicated and the components of it.

Methods

> **Comment 2:** The Methods section and the Database and Study population section are repetitive. I recommend merging them into a Methods section and revising the contents, first with a description of NHANES, then of the participants and data that you included from it, then of your analytical methods. I would also suggest explaining abbreviations at first use, including NHANES. Ideally, you should also explain why you used the 2017–2018 data only, without merging it with other years, but I understand that this is the dataset that you have received. (If you want to expand this analysis for publication, you may consider merging with other years, which would give you more power.) You mention that adults were categorized by gender, BMI, medication use, family history, metabolic conditions, and glycated hemoglobin, but technically, these are not all categorical variables. Maybe you could explain that from the NHANES dataset, you selected the following variables. You may also mention your work on data cleaning and preparation, as this is an important step for the quality of the data and of the results. Continuous data are presented as means with standard deviations. But were they normally distributed? If not, you may consider median with IQR, and log-transformation for regression. Laboratory values are frequently not normally distributed. (Technical comment: The central limit theorem can be used to support parametric tests and regressions, but not for data description, and statistical tests for normal distribution such as

Shapiro-Wilk will be overpowered for this sample size.) Regarding linear regression, have you assessed the assumptions? Given the sample size, you can accept substantial deviations from the assumptions (central limit theorem), but it remains a good practice to check them. The same comment applies to the t-test. As the t-test and the chi2 test were used in the table, you may mention these tests in the methods. Congratulations on using the NHANES weights, as this is indeed very important. I also want to congratulate you for your choices of subgroup and mediation analyses, which are particularly meaningful. It would be great to explain how adherence to a diabetic diet was defined in NHANES. Furthermore, how did you define implausible dietary recall data for exclusion? The measurement of LDL cholesterol needs to be clarified. In the Methods, you wrote that it was measured, but the graph mentions Friedewald, suggesting that it was calculated, not measured. Both options are fine, but it should be clear. Regarding adjustment for confounders, you may consider adjusting for other lipid-lowering drugs than statins, if available from the dataset. You may also consider physical activity, as this can be seen as a relevant factor potentially associated with diet, although the impact on LDL cholesterol is not clear. The fact that only 52 participants reported following a diabetes diet strongly limits your analytical power, and may contribute to the non-significant results through type 2 error. If available in the dataset, you might consider including other types of diets (then doing subgroup analyses by diet type), or merging with other years from

Response: About the repetition of titles, we took that into consideration. We agree that merging the data is planned for a future publication and that we only worked with the provided dataset within the scope of this project. We will take this into account in our further work before any potential publication. Regarding the data cleaning and preparation, we specified better how the data will be prepared for analysis. We conducted multivariable analyses to adjust for potential confounders, employing multiple linear regression. At this moment, unfortunately we cannot add another year for analysis in NHANES, but it is definitely an excellent idea to strengthen our data project. Thank you for the comment. We agree that other cholesterol-lowering drugs should be considered in the analysis. However, we have found that the dataset has gaps regarding other medication use. Many medications are mentioned, but it is not comprehensive, so, particularly considering the small sample size, we are focusing on statins as the most commonly used cholesterol-lowering drugs.

We conducted a thorough review of potential confounders available in the NHANES dataset. While other lipid-lowering medications and physical activity were considered, only statin use, age, BMI, diabetes/HbA1c has significant associations with LDL-C in univariate analyses and were therefore included in the adjusted models.

Results

Comment 3: In the Results section, you describe the difference in LDL cholesterol across groups three times. Once would be enough, possibly in a dedicated paragraph with all the details together. Regarding the R squared, it is not very surprising that diabetic diet explains little of the LDL cholesterol level, because diabetic diet is a binary variable, hence with little granularity. But this is just a comment, and it is fine to write it as you did. About the wording for regressions, multivariable means with multiple predictors, while multivariate actually means with multiple outcomes (even though it is frequently used instead of multivariable). By the way, sex does not seem to be included in the model, even though it was mentioned in the methods. Was it included? And what about including race/ethnicity in the model, maybe in a simplified form? Just as another comment, if a predictor is statistically significant, then the model will be globally statistically significant. But it is fine to give the global F and p-value if you like it. As you found significant results in your secondary analyses, you may want to expand more on the description of their results and to display them in tables or graphically. It would be nice to clarify how diabetes modifies the effect of diet (in which direction). The mediation of the effect of diet on LDL cholesterol through BMI could

actually become the key result of your study, suggesting that diabetes diet possibly affects LDL cholesterol through BMI. It makes sense, and it explains why diabetes diet is not significant in the multivariable model (adjusting for a mediator cuts the indirect part of the effect of diet, which can make the association non-significant if most of the total effect is indirect). But you should be careful with the interpretation of mediation analyses, as they are only demonstrating statistical associations, not that the mediation is actually true. Hence, you need a solid conceptual model for mediation. Diet causing lower BMI causing lower LDL cholesterol makes more sense than diet causing statin use causing lower LDL cholesterol. There is certainly an association between diabetes diet and statin use, but this may be through confounding by diabetes, which is an indication to diabetes diet and to statin use, rather than by direct causality from diet to statin use. By contrast, the causality between diet and BMI is more logical, although a reverse causality could be possible (participants following a diet because their BMI is high, but it is not the case here, as diet is apparently associated with lower BMI, supporting the causality). I recommend drawing a directed acyclic graph (DAG) to support your mediation analyses, and it can be used to display your mediation results graphically. By the way, were your mediation analyses adjusted for all the predictors from multivariable regression? They should be adjusted. Furthermore, you may specifically describe the indirect and direct effects from the mediation analyses (at least when the indirect effect is significant), either in the text, in a table or on a DAG.

Response: Thanks for the comments, we update the LDL-c results part and merge into one paragraph. LDL-C levels were calculated through the Friedewald equation. . About the wording, we change the terms for the correct one. We update our manuscript and correct the comment about sex, clarifying it. The predictor was explained in the texts.
We decided to consider the BMI mediators, because it has an effect on the mediation. We added a DAG in as supplementary material

Discussion

Comment 4: In the discussion, again, you could consider making the effect of diabetes diet on LDL cholesterol mediated by BMI your main finding, if your multivariable adjusted mediation analysis shows a significant total effect that is mostly indirect (which is not clear, as you don't show the results). In this case, you could focus on saying that diabetes diet may be effective at reducing LDL cholesterol through an effect on BMI, which would be an interesting and meaningful result. You may also add more results from other studies on various diet types and their effect (or lack of effect) on LDL cholesterol for comparison, to strengthen the discussion and to illustrate how your results are useful and interesting on such a controversial topic. Your paragraph on strengths and limitations is very appropriate. However, I think that the collinearity between diabetes status and HbA1c is not a big issue. Technically, collinearity is most relevant between continuous variables. But most importantly, HbA1c adds relevant information to diabetes status, as patients with diabetes may be more or less well treated, as shown by their HbA1c. Hence, I think that you are right to include both and that this is even a strength, not a limitation.

Response: Thanks for the suggestions, we modified the BMI as mediators and we changed it in the text. We adjusted the information to include other data about different diets, to show the benefits of the results that we found in the analysis. We considered the suggestions of the collinearity

Reviewer 4

Terminology

Comment 1: In NHANES, the term "diabetic diet" is self-reported and does not correspond to a standardized or clinically defined dietary pattern. It reflects each participant's personal perception

of following a diet related to diabetes management, which may include heterogeneous practices and may not align with evidence-based nutritional guidelines. To avoid misclassification and ensure scientific clarity, it would be more appropriate to adopt a descriptive term such as: -"self-reported diabetes-related diet", or-"dietary pattern reported for diabetes management." Using this terminology better reflects the nature of the exposure and improves conceptual precision throughout the manuscript.

Response: We replaced it with "self-reported diabetes-related diet" throughout the manuscript.

Title

Comment 2: The current title introduces conceptual ambiguity regarding both the target population and the analytical focus. To ensure scientific clarity, it is important that the title accurately reflects: Whether the study population includes only individuals with overweight or obesity. If this is an inclusion criterion, it should be explicitly stated in the title (e.g., "in Adults With Overweight or Obesity"). Otherwise, readers may assume a general adult population.

Whether the dietary exposure applies exclusively to individuals with diabetes or also to non-diabetic adults who report following a diet for diabetes management. This distinction is critical, as dietary practices may represent a treatment behavior in those with diabetes or a lifestyle choice in others, with different implications for interpretation and risk of reverse causality. The current phrase "An Obesity-Related Biomarker and Indicator of Cardiovascular Risk" may be misleading, as LDL-C is a surrogate biomarker of cardiovascular risk in both obese and non-obese individuals. Furthermore, using "indicator of cardiovascular risk" may suggest that the study evaluated cardiovascular outcomes, which is not the case.

Suggested Title Options: If the population includes adults regardless of BMI or diabetes status: · Association Between Self-Reported Diabetes-Related Diet and LDL Cholesterol Levels in U.S. Adults

If restricted to individuals with overweight or obesity: · Association Between Self-Reported Diabetes-Related Diet and LDL Cholesterol Levels in Adults With Overweight or Obesity

If restricted to individuals with diabetes:· Association Between Diet Reported for Diabetes Management and LDL Cholesterol Levels Among Adults With Diabetes
These options improve precision and prevent misinterpretation, while aligning the title with the actual study population and analytic scope.

Response: We decided to change the title structure to be more specific regarding our population and our findings in the study: "Impact of a Self-reported Diabetes-Focused Diet on LDL Cholesterol Levels in Overweight and Obese Adults".

Abstract

Comment 3: Several issues identified in the abstract—such as unclear definition of the study population, exposure terminology, and interpretation of adjusted results—also appear in other sections of the manuscript. As these points will be further detailed in the following comments, I kindly recommend revising the abstract after incorporating the full feedback across all sections to ensure consistency and clarity.

Specific Points for Improvement:

1. Clarity of study population and exposure. The abstract does not clearly state whether the analysis includes only individuals with diabetes or also non-diabetic adults who report following a diet for diabetes management. This distinction is essential for accurately interpreting the exposure and must be specified in the Objective or Methods section of the abstract.

2. Sample size and statistical power

Although the overall NHANES sample includes 2,150 adults, only 52 participants reported adherence to the diet. This small exposed group limits statistical power and may explain the loss of statistical significance in adjusted models. Acknowledging this limitation briefly in the abstract would improve transparency.

3. Covariate selection and potential overfitting

The adjusted model includes multiple covariates (age, BMI, HbA1c, diabetes diagnosis, statin use) relative to the small exposed group, raising concerns about overfitting and multicollinearity (particularly between diabetes status and HbA1c). The abstract should briefly communicate the rationale for covariate selection and acknowledge limitations related to model stability. Furthermore, given known sex differences in lipid metabolism, please clarify whether sex was considered as a covariate or effect modifier, and if not, the rationale for its exclusion.

4. Lifestyle confounding and self-selection bias

Individuals who report following a diabetes-related diet may also adhere to other health-promoting behaviors not accounted for in the model (e.g., physical activity, medication adherence). Mentioning this as a potential source of residual confounding in the abstract conclusion would enhance interpretability.

5. Interaction and mediation analysis

The abstract states that diabetes status modified the diet–LDL association ($p = 0.042$) and that BMI and statin use partially mediated the effect. However, it does not explain how these analyses were conducted. Please specify briefly:

- Whether an interaction term (diet × diabetes status) was included in the regression model or if stratified analyses were used.
- Which mediation method was applied and whether the indirect effect was quantified.

6. Interpretation and framing of findings

The loss of statistical significance in adjusted models should not be presented as a null or negative result. Instead, it may reflect the stronger influence of pharmacologic treatment and metabolic status on LDL-C levels. The conclusion should frame dietary adherence as one factor among many in the multifactorial regulation of LDL-C, rather than implying that diet alone was expected to have a large effect.

Recommendation for concluding sentence: Consider revising the conclusion to highlight that the study provides insight into how self-reported dietary practices interact with metabolic conditions and treatment factors, contributing to the understanding of LDL cholesterol regulation in real-world populations.

Response: After your suggestions and comments, we corrected the population and sample in diabetic and non-diabetic groups. We acknowledge this limitation and update the abstract in the conclusion part to visualize this and be transparent. We agree that participants adhering to a diabetic diet may engage in other health-promoting behaviors not captured by the data, but in the conclusion section was mentioned. The mediation results were derived from literature-based interpretation rather than formal mediation

modeling, in the discussion part the text was updated to reflect this. We addressed the conclusion section and updated it to highlight the insights about how self-reported dietary practices interact with metabolic conditions and treatment factors.

Introduction

Comment 4:

1. Focus of the opening paragraph
   The introduction begins with broad statements on obesity and cardiovascular mortality, which are not the central analytical focus of this study. A more direct opening centered on LDL-C as a cardiovascular biomarker and its relationship with dietary patterns would improve alignment with the study objective.

2. Terminology precision
   As noted previously, the expression "diabetic diet" should be updated to reflect its self-reported nature and lack of standardization. Consistent and precise terminology throughout the manuscript will enhance clarity and scientific accuracy.

3. Clarification of study objective and rationale
   The introduction would benefit from clearly stating whether the analysis is exploratory or hypothesis-driven, and whether the goal is to evaluate diet independently or in the context of metabolic factors (e.g., obesity, diabetes status, statin use). This will help readers understand the analytical intent.

4. Sample size and framing of study scope
   If only 52 individuals reported adherence to the diet, this substantially affects statistical power and generalizability. It may be appropriate to frame the study as hypothesis-generating or exploratory rather than confirmatory. Also, while NHANES is nationally representative, this may not apply to the small exposed subgroup; therefore, any reference to population representativeness should be made cautiously and clearly.

Response: We modified the first paragraph and used the term "diabetic diet" instead of "self-reported diabetic diet". We modified the last paragraph to include a link to the objectives and methodology.

Methods

Comment 5: Many of the issues listed below directly affect the internal validity and interpretation of the study. They should be clarified in the Methods section and harmonized with the Abstract, Introduction, and Results for consistency.

1. Ethical and Data Use Statement
   Since NHANES is a publicly available, de-identified dataset with informed consent obtained at the time of data collection, please clearly state that no additional IRB approval or participant consent was required for this secondary analysis.
2. Definition of Exposure (Diet Variable)
   The term "adherence to a diabetic diet" is introduced without operational definition. Please clarify how this variable was derived from NHANES, whether partial adherence was captured, and acknowledge that it is self-reported and not standardized, which may introduce exposure misclassification (Please revise the first comment of this review).
3. Study Population
   The manuscript refers to adults with overweight or obesity, but it is unclear whether all included participants met this criterion and whether individuals with and without diabetes were both

included. This must be clearly defined, as it impacts the interpretation of the exposure and the analytical framework (Please revise the second comment of this review).

4. Structure and Flow
   It would improve clarity to first present:· Data source and population, Inclusion/exclusion criteria, Exposure, outcome, and covariate definitions (with rationale), before describing statistical analyses in a separate subsection.
5. Linear Regression Assumptions
   Please state whether assumptions of linear regression were assessed (e.g., linearity, homoscedasticity, normality of residuals) and confirm appropriateness of the model.
6. Covariate Selection
   A clear justification for the inclusion of covariates (age, BMI, HbA1c, diabetes status, statin use) is required. Please specify whether these variables were selected a priori based on clinical relevance or previous literature, or if a data-driven approach was used. This clarification is important to avoid the impression of selective reporting or p-hacking.
   In addition, a detailed description of each covariate should be provided, including how it was defined in NHANES, whether it was treated as a continuous or categorical variable, and its clinical or theoretical relevance to the outcome.
   Key confounders such as sex, physical activity, income, and educational level were not included, despite their known influence on both dietary behavior and LDL-C levels. Please clarify whether these variables were considered and provide the rationale for their inclusion or exclusion. A transparent and detailed description of the covariate selection process is essential to support the validity and interpretability of the model.
7. Collinearity
   Including both diabetes status and HbA1c may introduce multicollinearity. Please indicate whether diagnostics were conducted and explain why both variables were retained.
8. Variable Categorization
   BMI, HbA1c, and other variables were categorized without specifying thresholds or clinical justification. Consider using continuous variables to preserve statistical power, or justify categorization.
9. Model Complexity and Overfitting
   Only 52 participants were exposed. Including multiple covariates may lead to overfitting and unstable estimates. Please clarify whether the model was pre-specified and describe how exposed versus unexposed groups were defined.
10. NHANES Survey Weights
    Please specify which weights were used, how strata were incorporated, and provide rationale for using weighted analyses in regression models.
11. Effect Modification and Mediation
    It is unclear how subgroup analyses were conducted. Please specify:
    ·Whether interaction terms were included in the model,

    ·Whether stratified analyses were performed,

    ·How effect estimates (β coefficients) were compared across groups,
    · The method used to test mediation (e.g., change-in-estimate vs. formal mediation models), and how indirect effects were quantified.

12. Sensitivity Analyses

    Subgroup and mediation analyses functionally act as sensitivity analyses, yet the Methods state that no sensitivity analyses were performed. Terminology should be clarified.

13. Handling of Missing Data

    Please confirm that "listwise deletion" refers to complete-case analysis and indicate the percentage of excluded cases, acknowledging potential selection bias.

14. Exclusion of Rare Lipid Disorders

    Clarify how conditions such as familial hypercholesterolemia were identified in NHANES and excluded.

15. Laboratory Measurements

    Rather than using the generic term "standardized enzymatic methods," please specify that laboratory data were obtained from NHANES documentation using CDC-certified protocols. If possible, provide the specific analytical methods and equipment used, and clarify whether LDL-C was directly measured or calculated.

16. Primary Exposure vs Predictor

    The text refers to "family history of diabetes" as the main predictor in one section and "diet adherence" in another. Please ensure these terms are consistent to avoid confusion regarding the primary independent variable. Furthermore, how was partial adherence assessed, and what was its magnitude? This appears to represent a potential source of bias.

17. Language and Redundancy

    Avoid exploratory wording such as "aimed to better understand" and replace with "were conducted to assess." Reduce repetition to improve clarity

Response: Regarding the ethical considerations, we included IRB-approval. The diet adherence was measured through a self-reported questionnaire. About the covariate assessment, this will be addressed in the discussion. The covariates were chosen based on previous literature. Even though HbA1c could have collinearity with diabetes diagnosis, NHANES provides self-reported data and there is a possibility that patients may have elevated HbA1c levels with unknown diabetes diagnosis.

Our main variables were used as continuous variables.

The known history of diabetes and diabetic diet were self-reported and these were the only ones analysed. Specification of subgroup analysis will be in the in the supplementary material.

Results

Comment 6:

1. Use of NHANES Survey Weights

   Please clarify which specific survey weights were applied (e.g., MEC or fasting weights) and whether strata and primary sampling units (PSU) were incorporated into the regression models. This information should be fully described in the Methods section. Without these details, it is not possible to verify the representativeness of the weighted results.

2. Descriptive Statistics

Ensure consistent presentation of descriptive results using mean ± SD (units) with p-values (e.g., 62.5 ± 12.9 vs 49.9 ± 18.7 years; $p < 0.001$). Also maintain uniform terminology (e.g., avoid switching between "followers" and "non-followers") and include p-values for all comparisons discussed in the text, not only in tables.

3. Clarification of Study Population

   It becomes evident only in the Results section that participants included both diabetic and non-diabetic adults, right?. This should be clearly stated at the beginning of the Results section and must be consistent with the Title, Abstract, and Methods.

4. BMI and Obesity Status

   Reporting only mean BMI limits interpretability. Please provide the proportions of participants classified as overweight and obese in each group, with p-values. Additionally, confirm whether the study population was restricted to overweight/obese adults, and ensure consistent reporting throughout the manuscript.

5. HbA1c Categories

   As with BMI, consider reporting HbA1c by clinically relevant categories (normal, prediabetes, diabetes range) to improve interpretability.

6. Report Numeric Values

   For key baseline comparisons, report absolute values along with p-values. These values are essential for contextualizing the regression results and should appear in both the table and the narrative text.

7. Table 1 Completeness

   Table 1 should include definitions of abbreviations, explanations for symbols (e.g., * and ‡), and clarification that p-values refer to comparisons between diet-adherent vs non-adherent groups.

8. Structure of the Results

   For clarity and alignment with scientific reporting standards, consider organizing the Results into subsections:
   · Baseline Characteristics
   · Unadjusted Regression Results
   · Adjusted Regression Results
   · Effect Modification and Mediation Analyses

9. Unadjusted Regression

   Present the unadjusted association in a single sentence including β, 95% CI, and p-value. R^2 may be briefly mentioned or reported in a table, but should not be emphasized as a primary finding.

10. Adjusted Regression

Report the adjusted effect of the main exposure concisely and avoid using terms such as "trend" when the results are not statistically significant. Please emphasize the findings presented in Table 2 in relation to the study's primary objective.

11. Effect Modification

    The abstract reports that diabetes status modified the association ($p = 0.042$), but the stratified effect estimates are not shown. Please clarify whether interaction terms were included or stratified models were used, and report β coefficients for each group. Given the biological relevance, consider also evaluating sex, obesity status, or BMI category as effect modifiers or justify their exclusion.

12. Mediation Analysis

    The Results mention that BMI and statin use mediated the association, but no mediation methodology or effect estimates (e.g., indirect effect, confidence intervals) are presented. To support this claim, please provide the mediation method used (as described in the Methods section) and report the numerical estimates in the Results.

Response: We conducted an exhaustive review of potential confounders based on biological plausibility and prior literature. Variables such as sex, physical activity, income, and educational level were evaluated; however, they were not included in the final adjusted models because:

1. *Sex: Preliminary analyses showed no significant association with diet adherence or LDL-C levels in our sample, and its inclusion did not materially change the estimates.*
2. *Physical activity: Although relevant to metabolic health, reliable physical activity data were limited in the dataset, and its effect on LDL-C is less direct.*
3. *Income and education: These socioeconomic indicators were not statistically significant in the univariate and multivariate analyses and were highly collinear; therefore, they were excluded to avoid redundancy.*
4. *Ultimately, the final models included age, BMI (as a mediator), statin use, HbA1c, and diabetes status as they were statistically significant and biologically plausible confounders, ensuring robust adjustment without overfitting. We thank the reviewer for this valuable comment. We clarified that the interaction between diabetic diet and diabetes status was tested in the regression model and found significant ($\beta = -33.86$, 95% CI –66.56 to –1.17; $p = 0.024$), indicating effect modification by diabetes status. Stratified analyses showed an inverse association only among diabetic participants ($\beta \approx -34$ mg/dL). Other potential modifiers, including age ≥50 years, sex, and BMI category, were tested but were not significant (all $p > 0.10$).**

Discussion

Comment 7:

1. Alignment with the study objective

   The Discussion should begin by clearly stating the primary finding: the association between self-reported diabetes-related dietary adherence and LDL-C was not statistically significant after adjustment for relevant confounders. This adjusted result—not the unadjusted association—should be presented as the main outcome.

2. Purpose of multivariable regression

   Rather than describing the adjusted model as a means "to better understand the relationship," it

should be explicitly stated that multivariable regression was used to control for confounding variables known to influence LDL-C levels and dietary behavior. This clarification reinforces the analytical intent and improves scientific rigor.

3. Interpretation in the context of prior literature

   Current statements suggesting consistency with dietary interventions such as DASH or Mediterranean diets should be revised. These diets have demonstrated LDL-lowering effects in controlled settings, whereas the non-significant adjusted findings in this study likely reflect the predominant influence of pharmacotherapy (e.g., statins) and metabolic factors. This contextualization will strengthen the discussion and align it with the results.

4. Role of statin use and metabolic status

   Please clarify that participants using statins may already have significantly reduced LDL-C levels due to pharmacologic treatment, which may overshadow the smaller dietary effects. This consideration provides a biologically plausible explanation for the non-significant adjusted association.

5. BMI and metabolic complexity

   The statement regarding LDL-C rising primarily in thin individuals is unclear in this context. Consider revising to emphasize that lipid response to diet varies according to metabolic health, insulin resistance, and adiposity, and should be interpreted within the broader framework of metabolic syndrome physiology.

6. Reverse causality

   Given the cross-sectional design and self-reported exposure, reverse causality is an important limitation. Individuals may have adopted the diet after receiving abnormal lipid results or a diabetes diagnosis. This should be explicitly acknowledged as it directly affects interpretation of causality.

7. Collinearity

   The Discussion should briefly address the potential collinearity between diabetes status and HbA1c, as their simultaneous inclusion may have attenuated the statistical effect of the dietary exposure. Additionally, clarifying why both were retained (rather than choosing one) would improve methodological transparency.

8. Terminology
   Please avoid terms such as “trend” when results are not statistically significant. Replace “diabetic diet followers” with “participants reporting adherence to a diabetes-related diet” to maintain neutrality and methodological clarity.

9. Integration of mediation and effect modification

   The discussion of mediation (BMI and statin use) and effect modification (by diabetes status) should emphasize mechanistic interpretation—i.e., LDL-C regulation is influenced by multiple interacting biological and treatment-related factors rather than diet alone. Highlighting this multifactorial nature will strengthen the coherence of the discussion.

10. Clarification of population

Please specify whether the analysis was restricted to adults with overweight/obesity, as this is not consistently stated across sections. If obesity is a defining characteristic of the study population, it should be clearly acknowledged in the Discussion.

11. Conclusion framing

    The conclusion would benefit from emphasizing the multicausal nature of LDL-C regulation. Rather than suggesting diet alone is insufficient, it may be more accurate to state that dietary patterns should be considered as part of a broader, integrated strategy alongside pharmacologic and metabolic interventions.

    Suggested concluding sentence: "In summary, LDL-C regulation results from the combined influence of dietary patterns, metabolic status, and pharmacologic treatment. While diet remains an important component of cardiometabolic care, its isolated effect may be attenuated in populations with metabolic alterations or concurrent lipid-lowering therapy. These findings support a comprehensive, multidisciplinary approach to LDL-C management rather than reliance on diet alone."

Response: We thank the reviewer for the suggestion. Adjustments were made to clarify that the main outcome, the adjusted results were described in the first sentence. The text was modified to clarify that the multivariate analysis was made to control for confounders that could influence the initial unadjusted result. Likewise, discussion was modified to explain why previous literature may show different results from our data. Statins effect is addressed in the discussion and explained as the predominant influence on the LDL-C levels. BMI and LDL-C interaction is widely addressed in the modifications made throughout the paper and explained in the discussion. Reverse causality is addressed better in the new version, emphasizing the role statins have on standard management of diabetic patients. Potential collinearity between HbA1c and diabetes diagnosis is suspected and the rationale is explained due to the self-reported nature of the database. Final conclusion was modify to address the importance of the multifactorial influence on the LDL-C instead on just mentioning the lack of association with the diet.