Author's response to reviews

Title: Nut Consumption and Risk of Atrial Fibrillation in the Physicians' Health Study

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Author's response to reviews: see over
Nehme Gabriel, MD,

Editor-in-Chief,

NutritionJournal

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Dear Dr. Gabriel,

Thank you for the opportunity to revise our work again. We have attached a copy of the revised letter with all the changes highlighted in red. Thank you for your very thorough review and helpful comments and for the opportunity to improve our work. Our responses to the comments raised by the reviewers are included below. We have meticulously addressed all concerns raised by the reviewers and hope that our work is now deemed appropriate for publication.

Sincerely,

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Reviewer 1 (Kenneth J Mukamal):

Major Compulsory Revisions

1) The authors have generally responded adequately to my concerns. I have one remaining minor revision. I would like to see the results of the post hoc analysis that both reviewers hint at, namely the comparison of all weekly use with lesser use. Given that this data is available to the authors, the comment in the paper that this would be interesting seems to miss the opportunity to answer the question.

Done. We have included the following statements in the statistical analysis, results, and discussion sections respectively:

*In an additional analysis using the same multivariable model we dichotomized nut consumption into ≥ weekly versus < weekly to see if it modified the relation between nut consumption and AF.*

The multivariable adjusted hazard ratios (95% CI) for incident AF using nut consumption as ≥ weekly versus < weekly was 1.07 (0.99-1.15).

The results indicate that although the power was limited at the levels of nut consumption that would be most likely to influence AF risk, there was a non-statistically significant increase in AF risk among all consumers of nuts weekly or more. As a post hoc analysis, this would therefore be an interesting analysis for other data sets.
Reviewer 2 (Maira Bes-Rastrollo):

**MAJOR COMPULSARY REVISION:**

1) I do not understand why the authors in the new version of the multivariable models they adjusted also for nut consumption, their main exposure of interest. Please, correct it.

Done. The typographical error has been corrected.

**MINOR REVISIONS:**

2) The authors have not included in another color the information about the flowchart of participants. Consequently, it seems that this information was not missing in the previous version (Just a comment).

Done. It has been highlighted in red in this version.

3) In the new version of the manuscript, in the results section, I would include in the last paragraph: Results of sensitivity analysis "excluding those who developed any chronic disease such as any cancer, DM, or CVD" did not alter the results either...
4) The authors should include the crude way to assess physical activity as a potential limitation for residual confounding in the Discussion section.

Done. We have included the following sentence in the discussion section:

The crude way of assessing physical activity was also a potential limitation in our analysis and could have lead to residual confounding.

5) Regarding the answer to the question number 8, I do not understand why the authors mentioned that the risk it appears that might even be statistically "increased" when the results of multivariable analysis showed the estimation for the hazard ration below the null value.

Additional analysis was conducted per other reviewer’s suggestion using nut consumption as dichotomous variable i.e. > weekly versus < weekly. Based on the analysis following statements were included in the statistical analysis, results, and discussion sections respectively:

In an additional analysis using the same multivariable model we dichotomized nut consumption into > weekly versus < weekly to see if it modified the relation between nut consumption and AF.
The multivariable adjusted hazard ratios (95% CI) for incident AF using nut consumption as ≥ weekly versus < weekly was 1.07 (0.99-1.15).

The results indicate that although the power was limited at the levels of nut consumption that would be most likely to influence AF risk, there was a non-statistically significant increase in AF risk among all consumers of nuts weekly or more.

6) Please include in the Discussion section of the new version of the manuscript that you do not have available information on family history of hypertension, hypercholesterolemia, or diabetes, as a potential limitation of the study.

Done. We have included the following sentence in the discussion section:

We did not have information on family history of hypertension, hypercholesterolemia, or diabetes and therefore were unable to adjust for it.

7) In Table 1, authors should mention, how they define “Physical activity”.

Done.