Author’s response to reviews

Title: Adherence to the Low Carbohydrate Diet and the Risk of Breast Cancer in Iran

Authors:

bahareh sasanfar (bsasanfar@yahoo.com)
fatemeh toorang (f.toorang@gmail.com)
Ahmad Esmaillzadeh (a-esmaillzadeh@tums.ac.ir)
Kazem Zendehdel (kzendeh@tums.ac.ir)

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Author’s response to reviews:

Dear Dr. Brady and Mulligan,

Thank you very much for your letter informing us of your decision regarding the manuscript (NUTJ-D-19-00184) entitled “Adherence to the Low Carbohydrate Diet and the Risk of Breast Cancer in Iran”. The manuscript has been revised according to the reviewers’ comments. Responses to the reviewer’s comments have been provided below. Revised texts have been highlighted. Thank you so much in advance.

Yours Sincerely,

Ahmad Esmaillzadeh, PhD

Department of Community Nutrition,
School of Nutritional Sciences and Dietetics,
Tehran University of Medical Sciences,
Tehran, P.O. Box 14155-6117
Iran
Tel:+98-21-88955805
Fax:+98-21-88984861
Email: a-esmaillzadeh@tums.ac.ir
Responses to Associate Editor Comments:

Associate Editor:
*This paper is generally clear and well-written, yet some grammatical errors occur throughout.

Authors: Thank you. We tried our best to do these errors in the revised version.

*The authors are usually, but not always, careful about stating the results of logistic regression models as "odds", but they do occasionally state these results as "risk"; please change to "odds".

Authors: Agreed. Done

*I agree with Reviewer #1 that the authors did not present the results of the analysis they conducted using the data from the other macronutrients. Why was this mentioned in the methodology but not analyzed?

Authors: Low carbohydrate diet is a specific dietary pattern. However, to construct this dietary pattern based on scoring method, all three major macronutrients are used. In other words, individuals with the greatest adherence to low carbohydrate dietary pattern are those who take the highest energy from fats and proteins, but the lowest percentage of energy from carbohydrates. Therefore, as you see, all macronutrients were used in this dietary pattern.

Responses to Reviewer 1

Reviewer #1: Sasanfar et al have examined the association between consumption of a low carbohydrate diet and incidence of breast cancer. The manuscript is clearly written, the data are of interest and the limitations of the current study are properly laid out by the authors. The current work is also clearly contextualized into findings from previously published research articles. The manuscript should be carefully read and edited as several sentences (listed below) appeared fractured.

Lines 10-11: it is not clear that protein consumption and fat consumption quintiles were calculated and scored separately. As written, it seems that they were scored together, making the range of 3-15 for final scores not immediately evident.

Authors: Agreed. The mentioned sentences were re-written to reflect this.
"Then, individuals in the highest quintile of fat were given the score of 5 and those in the lowest quintile of this macronutrient were given the score of 1. Participants in the other quintiles of this macronutrient were given the corresponding score. The same scoring method was also applied for dietary protein intake ".

Lines 76-77: this sentence does not make sense, please recheck.
Authors: Agreed. Re-checked

"We asked patients to report their dietary intakes in a year before diagnosis of breast cancer".
Line 193: "explain" should be added. This might further help explain the difference in findings.
Authors: Thank you. Added.

Lines 223-224: sentence needs editing.
Authors: Agreed. Done.

" Second, misclassification of participants in terms of dietary intakes cannot be excluded due to the use of FFQ in the current study"

Lines 225-226: "of the tumor" should be added. Fourth we did not have information of the hormone receptor status of the tumor for the participants.
Authors: Agreed. Added.

Responses to Reviewer: 2

Comments to the Author
Reviewer #2: In general, the manuscript was well-written and informative, providing clear descriptions of how the score was calculated and the study results. The paper requires editing due to language issues, so that it flows better and is easier to read.
Lines 79 - 81: presumably the average daily intake of a participant's own portion size was then calculated and the energy and nutrient intakes subsequently from this amount? Can you provide some information on how often this occurred, what foods were quantified using an alternative portion to the standard serving size, was it more usual in cases and controls, does this affect the validity of the FFQ?

Authors: Routinely, all the participants completed the questionnaire based on the given portion sizes. Individuals who could not report their frequency consumption based on the mentioned serving sizes were requested to report the frequency considering their own portion sizes and then the dietitians converted these portion sizes to those that were mentioned in the original FFQ. This was rarely happened and only small number of participants (say less than 50 people in the whole study population), mostly those aged older than 70 years, reported alternative portions. Therefore, this is unlikely to affect the validity of FFQ. This was added to the revised version.

How did you decide on your adjustment variables?

Authors: All the adjustment variables we used in the models were selected based on earlier literature.

There are a number of limitations to this study, which the authors have acknowledged, which may have had an effect on the findings: the lowest % energy from CHO was 41.5%, which is not low, compared to other studies; the possibility that cancer participants may have recalled their diet differently; and the sample size in some of the stratified quartiles by menopausal was quite small.

Authors: Thank you. It must be kept in mind that Iranians take most of their energy from carbohydrates and the average percent of energy from carbohydrates in the whole country is more than 60%. Therefore, 41.5% in the lowest category seems low for Iranians. This was highlighted in the revised version. Other limitations like the possibility that cancer patients might have recalled their diet differently compared to healthy population as well as the effect of their current condition on the recalled diet were also added. We agree that the sample size in some of our stratified analyses was small. This was also added.