

Author's response to reviews

Title: Repeatability and measurement error in the assessment of choline and betaine dietary intake: the Atherosclerosis Risk in Communities (ARIC) Study

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Editor-in-Chief

Nutrition Journal

Dear Sir/Madam,

We are pleased that you have reviewed our manuscript, Repeatability and measurement error in the assessment of choline and betaine dietary intake: the Atherosclerosis Risk in Communities (ARIC) study, for possible publication in Nutrition Journal.

This paper is a secondary analysis of the ARIC prospective cohort study. The related ARIC manuscript proposal #1049 was approved on October 7th 2008 and this paper has undergone NHLBI review and approval on October 15th 2008. We attest to the fact that each author has contributed to the conception and design of the work or the analysis of the data in a manner substantial enough to take public responsibility for it. Dr. Steven H. Zeisel, one of our co-authors who have been

omitted with our initial submission, has been added to the list of authors.

We thank the two reviewers, the editor, and the editorial office for their constructive and helpful comments. We have incorporated the changes suggested and briefly present our responses below.

Reviewer: Dr. Mihai D. Niculescu

1. a. Because at the time of our investigation no software was available to directly compute the total dietary intake of choline and betaine for individual participants, we composed our own algorithm as follows. For each of the ARIC FFQ items, the FFQ nutrient database that was created contained choline and betaine micronutrient content per 100 g/food. Thus, the total micronutrient content of each food item and for every nine possible ARIC FFQ frequency consumption answers (from “almost never” to “more than 6 per day”) was calculated. The micronutrient average daily intake for each study participant was obtained as the nutrient content for each FFQ food item times its frequency, summed over all FFQ items. The nutrient content of each food item was calculated as the product of the food micronutrient content (expressed in mg per 100 grams of food) and the food quantity, expressed in grams, in each FFQ food item. For frequency weights, a weight of 1.0 was assigned to once a day and proportional weights to the other responses, that is, “2-3 times a day” = 2.5. The quantities of food, expressed in grams, in each of the ARIC FFQ items were estimated using the Nutrition Data System for Research (NDS-R), version v5.0/35, developed by the University of Minnesota. Each ARIC FFQ food item was entered as an individual food.

For quality control /quality assessment purposes, we interacted with the Willett group at Harvard University. Because we used, to construct our nutrient database, the Minnesota database while they used the Harvard database, the Harvard group compared the intake of choline between the ARIC FFQ and the Nurses Health Study (NHS) 1980 FFQ (also a short version of the Willett FFQ). They calculated the daily intake of choline if each participant ate each FFQ item once per day. The values were similar between study populations. Specifically, the daily intake of choline if each participant ate every FFQ item was 1,493 mg in ARIC and 1,443 mg in the NHS 1980.

b. Because during the second ARIC examination (Visit 2) there was not possible to assess diet on all study participants, it was decided by the ARIC Steering Committee to assess it only in a random sample of about one thousand participants. This subsample assessment coupled with the corresponding assessment on the same participants during the ARIC baseline visit became the ARIC Dietary Assessment Repeatability Study.

2. The reviewer is right in pointing the relative inaccurate assessment through our dietary tool. We reported the estimated intake of choline and betaine (Table 3) with the awareness of the fact that a food frequency questionnaire is notorious in underestimating the actual intake for a specific nutrient, as evident in our total energy intake estimate (Table 1). The reliability coefficients presented in our

Table 2 are to be interpreted as an indication of the error magnitude of those actual intakes. In other words, the real intake of choline for a specific participant (as well as the average) could be almost twice that assessed by our FFQ; as indicated by the 0.5 reliability coefficient. We incorporated this specification within our discussion section.

Minor essential revisions:

We made a series of language corrections in order to improve the flow of reading. We considered the suggestion to add pertinent references in our background section. We also edited the text to be evident that we used the AI only for comparison purposes. Finally we better described the relationship between EAR and DRI.

Reviewer: Dr. Eunyong Cho

Major:

1. Although one of the aims of our analysis was to estimate the dietary intake of choline and betaine in the entire ARIC bi-ethnic population, we agree with the reviewer that it may be misleading to start the abstract methods with the entire cohort description. Accordingly, we rewrite that portion of the abstract to reflect this aspect.
2. We rewrite that paragraph to better reflect those facts (the estimates in a series of US populations) and highlight those studies.
3. As we mentioned during our response for the previous reviewer, because during the second ARIC examination (three years after the baseline visit) there was not possible to assess diet on all study participants, it was decided by the ARIC Steering Committee to assess it only in a random sample of about one thousand participants. This subsample assessment coupled with the corresponding assessment on the same participants during the ARIC baseline visit became the ARIC Dietary Assessment Repeatability Study. We clarified the portion of the methods section to better reflect that. Thank you for pointing it out.
4. The reviewer is raising an important aspect of a nutritional epidemiology investigation. We adjusted the nutrient intakes for both visits for total caloric intake and revised the results presented in Table 1.
5. The matrix covariance structure that was used in our simulations for the reliability coefficients presented in Table 2 provided the structure for de facto adjustment of every of the dietary variables on each of the other three. Therefore, our algorithm is already indirectly adjusting for caloric intake; actually, this was the main reason for which we decided to use total caloric intake in our covariance matrix.

In summary, we have responded to the Reviewer #1 and Reviewer #2's comments and we hope that the article will now be acceptable for publication. If I may be of any further assistance, please let me know.

Thank you in advance!

Sincerely,

Aurelian Bidulescu, MD PhD MPH (corresponding author)