Reviewer's report

Title: Usual choline and betaine dietary intake and occlusive coronary events: the Atherosclerosis Risk in Communities (ARIC) study

Version: Date: 19 March 2007

Reviewer: Majken Karoline Jensen

Reviewer's report:

General
This is a well-written paper on the association between estimated dietary intake of choline and betaine and risk of CHD among 14,430 men and women from the ARIC study. It is the first observational study of choline and betaine in relation to CHD since the reference values have become available in the US nutrient composition database. The authors used appropriate methods to explore the association and further included results after measurement error correction.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
1. Confounder adjustment: Because meats, eggs, and milk are important contributors to choline and betaine intake, it is important that all analyses are adequately adjusted for intake of saturated fatty acids, processed meats and other dietary confounders. Some sensitivity analyses could be performed (and discussed) that ensures the reader that the suggestion of a higher risk associated with the highest intake is not due to confounding from uncontrolled dietary factors.

2. Since this is a prospective study following the entire study population from baseline until CHD or end of follow-up, the comparison of intake at baseline between cases and controls is not that relevant (as for a case control study). More important for the reader, is the ability to note characteristics of the cohort itself that may be important modifiers of the association (Eg. the results could be different in a population with higher or lower intakes of folate, alcohol etc., and it is important to consider the results in that context). I suggest the authors replace table 1 with a table that shows the distribution of important baseline characteristics of the study pop. according to gender.

3. The discussion on effect-modification by folate or alcohol intake seems very explorative. Either more emphasis should be put on the importance of these investigations, or Table 3 should be deleted. Authors could note that they did not see any statistical evidence for interaction. The second paragraph on page 8 does not describe interaction with folate intake. A p-value of 0.08 is mentioned and a non-significantly higher risk among those with highest choline intake is mentioned among participants with low folate intake. –But in order to understand this statement the reader also needs to know the risk observed among those with high folate intake. Table 3 does not seem to provide very strong suppor for any interactions and all estimates have extremely broad confidence intervals. Also, the sentence ‘alcohol emerged as an effect modifier’ is not supported by the table.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
1. The description of the ARIC study on page 5 should include the year of baseline examination.

2. It is unclear whether or not diet was only assessed once in the ARIC study, or if the authors left out information from subsequent examinations.

3. Given that this is the first report on usual intake of choline and betaine in the average diet of a study population, a table showing the top 10 food items (and the mg per serving) on the FFQ that contribute to the intake of these two micronutrients in the ARIC population would be of interest (in addition to the sentence regarding this on page 7). The authors briefly discuss the risk for underestimation because their FFQ only included 66 items. Do they think the list of contributing foods would be different had the FFQ covered more foods?
4. On page 5, the authors state: ‘we considered the intakes of choline and choline plus betaine, in
continuous multivariable models’. It is unclear what is meant here because all results are presented in
quartiles.

5. Given the sex-differences in choline metabolism, it would be useful to present the gender-specific results
to the reader rather than state there wasn’t significant interaction (which could also be due to the low
statistical power).

6. The analyses stratified by the year of mandatory folate fortification are interesting. It is my belief that
many producers already initiated fortification of grain products earlier. Perhaps the cutpoint should be set at
an earlier time? It would be most appropriate if the authors are able to show results among subgroups of
cases that occurred both before 1996 and after (not only after folate fortification as the paper is now).

Discretionary Revisions (which the author can choose to ignore)

1. Consistency between the used term ‘occlusive coronary events’ in the title and ‘CHD’ throughout the
paper.

What next?: Accept after minor essential revisions

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests