Reviewer's report

Title: Maternal fish and shellfish consumption and respiratory and allergic outcomes at age two: A prospective cohort study in Brittany, France

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Reviewer: Torbjorn Oien

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The study is a cohort study in which maternal exposures before pregnancy (fish and shellfish separately/in combination) were related to clinical outcomes at age 2 years. The finding is that intake >1 time a month of shellfish before pregnancy is associated with increased risk of food allergy at age 2 years. No consistent association between fish intake and allergy related diseases were found.

Major Compulsory Revisions

Introduction
1. The aim of the study must be corrected, “effect” must be replaced with “association” or “impact” as this is an observational study. I would also suggest to substitute “respiratory and allergic outcomes at age two” with “allergy related diseases at age 2” as there are no biologic markers for allergic sensitization in this study.

Methods
2. A great concern with this study is the attrition, only 50% of the eligible parents responded to the questionnaire at 2 years. This is discussed in the text. Please include a table comparing baseline characteristics between losses to follow up and complete cases.

Assessment of respiratory and allergic outcomes
3. Another major concern is the assessment of the outcome variables, wheezing, atopic dermatitis and food allergy.

Two of the wheeze questions are validated questions from the ISAAC protocol, but the wording is not accurate, and reference #17 is an article on 13-14 years old children. Are these questions validated for children at 2 years? The last three questions are not validated (at least no reference given) “Yes” to one of the first four questions classified the child in the “certain wheeze” category, whilst “yes” to the fifth question classified the child in the “probable wheeze” category. Why introduce 3 categories for wheeze? I think this will dilute the “wheeze” endpoint, and many children will be misclassified and possible associations can be lost. I would suggest that the authors reclassify “wheeze” in two categories and do binomial logistic regression also for wheeze.

4. The authors uses the term “atopic dermatitis”. As no information on atopic status are given, I suggest it should be replaced by “eczema” according to the
WAO classification.

5. Atopic dermatitis was identified by a positive answer to both of the following questions (from the ISAAC questionnaire): “Has your child ever had an itchy skin rash, which was coming and going?” and “If yes, has this itchy rash affected any of the following places - the folds of the elbows, behind the knees, in front of the ankles, under the buttocks, or around the neck, ears, or eyes?” In small children eczema often starts on the extensor side, are these children missed? Please clarify.

6. I also have concerns about the assessment of “food allergy”. What is meant by “medical diagnosis of milk/food allergy” do they have elevated sIgE, or are a food challenge test performed? If not they are at the risk of misclassification.

Statistical analyses

7. Fifteen covariates are used in the regression analyses; few of them are associated to the outcome variables. Are the covariates tested for interaction? Please clarify why all covariates are in the regression models.

8. No information is given for the multiple imputations. The predictor variables used for multiple imputations should be stated.

Results

9. Table #3 is missing

Discussion

10. Page 10, second paragraph, second sentence: “To our knowledge, no study has assessed its association with food allergy.” Calvani M et al. Pediatr Allergy Immunol. 2006 Mar;17(2):94-102: Consumption of fish, butter and margarine during pregnancy and development of allergic sensitizations in the offspring: role of maternal atopy. Calvani concludes that “frequent maternal intake (‘2-3 times/wk or more’) of fish reduced the risk of food sensitizations by over a third (aOR 0.23; 95% CI: 0.08-0.69).” This article with an opposite result should have been a part of the discussion.

11. There is no information on the children’s diet. At what age was fish introduced in the children’s diet, and how much fish did they eat? Are maternal and children’s diet intercorrelated regarding fish and shellfish in Brittany? Is it possible to draw conclusions about the importance of maternal seafood intake before pregnancy when the children’s diet not is accounted for?

Minor Essential Revisions

1. Page 7, use SD instead og +/- reporting the age of mothers and children
2. Page 8, second paragraph: Clarify if the ORs are adjusted or imputed.
3. Reference #20: Only the abstract is in English, and I can’t see that the information in the abstract supports the statement, second line page 10.
Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.