Reviewer's report

Title: A Prospective Study of Dietary Selenium Intake and Risk of Type 2 Diabetes

Version: 2 Date: 17 August 2010

Reviewer: Simin Liu

Reviewer's report:

This prospective study assessing the relation of dietary selenium intake to the risk of type 2 diabetes among a cohort of 7,182 Italian women addresses a potentially important area related to nutrition and risk of type 2 diabetes. The revised manuscript is well-written and improved from the first version, and the authors have addressed many of the reviewers' concerns.

The magnitude of the observed associations seems fairly strong for one nutrient that clearly interacts with many other demographic, lifestyle, and dietary factors in influencing the risk of metabolic disease. The discussion acknowledges that unmeasured confounding cannot be ruled out, but it may be worthwhile to stress the importance of interactions and the limitations of assessing the role of one nutrient in relation to a complex metabolic disorder. Also, alternate explanations for the observed associations should be emphasized more explicitly (see below).

Major Compulsory Revisions:

None.

Minor Essential Revisions

1. Discussion: Although biological mechanisms are speculative at this point, it may be useful to elaborate a bit more how high selenium intake could increase the risk of diabetes. Although selenium is toxic at very high levels, levels of selenium based on dietary intake were far below values considered toxic.

2. Discussion: The discussion of misclassification is quite vague and would benefit from a more specific description of how biases might be operating in this study setting.

3. Table 1: Suggest that you remove reference to “cases” for the “Non-diabetics cases” and instead refer to them as “Non-diabetics.”

Discretionary Revisions

4. Statistical Analysis: It may be interesting to examine interactions with smoking and alcohol intake.

5. Statistical Analysis/Discussion: According to Table 2, red meat has a much higher level of selenium than any other food, including other sources of animal
protein. Red meat has been positively associated with type 2 diabetes among women in prospective settings (Song et al, Diabetes Care, 2004), and contains preservatives, additives, and nitrates as well as saturated fat and cholesterol, all factors that may increase the risk of diabetes. It may be that these other factors found in red meat and correlated with selenium are actually driving the observed associations in the current study. Have you examined the correlations between selenium intake and any of these other components? Also, it may be worth mentioning this point in the context of unmeasured confounding in the Discussion section.

6. Statistical Analysis: Given the likely high correlation between dietary components, did you check for multicollinearity issues in your models?

7. Statistical Analysis: Do you have data on fruit and vegetable intake to include in the model?

8. Statistical Analysis: Suggest fitting a quadratic spline model to explore the shape of the trend across the range of selenium intake.

**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.