Reviewer's report

Title: A case-control study of glycemic index, glycemic load and dietary fiber intake and risk of adenocarcinomas and squamous cell carcinomas of the esophagus: the Australian Cancer Study

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Reviewer: Veronika Fedirko

Reviewer's report:

This is a well written manuscript describing a large population-based case-control study of three esophageal cancer sub-types and dietary factors (glycemic index, glycemic load, dietary carbohydrate, and dietary fiber intakes). The supplementary data were not available for download, hence it was not reviewed. Specific comments are included below.

Major Compulsory Revisions

1. Male sex is the major risk factor for esophageal cancer. The results for men and women should be presented separately, if not in the text of the paper, then in the supplementary material.

2. Detailed adjustment for smoking is important. The variable that the authors are using wouldn’t completely account for smoking duration and status, e.g. former smoker category is not included. If data and sample size permit, a combination variable that takes into account smoking duration, intensity, and status would be preferable (e.g., never, former <10 and #10 years, current <15 cigarettes/day, >…).

3. Have the authors considered other methods for energy adjustment, e.g. nutrient density? Where the results from the other methods to adjust for energy similar to the ones presented?

4. The GI should not be energy adjusted since GI values reflect the physiological response to the consumption of the food item, but not its quantity.

5. What were the main food sources of total starch, sugars and dietary fiber? The results of analyses by food source, particularly, for dietary fiber would be interesting to include.

6. It is not clear whether sugar, starch, and fiber were mutually adjusted for each other in the models.

7. Previous paper by George et al 2009 suggested the association between GI and esophageal cancer is modified by red meat intake, and among men possibly by saturated fat intake. It would be interesting to consider these variables as potential effect modifiers in the present study.

8. Potential effect modification by diabetes status and acid reflux symptoms was not explored. Is having acid reflux symptoms associated with a change in diet? If
it does, then it could be an effect modifier of the association between dietary variables and esophageal cancers.

9. Sensitivity analysis excluding individuals with diabetes would be appropriate.

10. Tables 2-3: In the Stat methods, it was mentioned that the quartiles were sex-specific. However, in the tables, it looks like the median and range for each quartile are for men and women combined, whereas they should be presented separately for men and women. It is also not clear whether men and women have different distributions of dietary variables (usually women have lower GI/GL intakes compared to men).

11. Cancer stage information is not shown in Table 1 or in the text. It would be interesting to see the distribution by stage for each type of cancer. It is possible that undiagnosed advanced disease is associated with weight loss and dietary changes that occurred >1 year before cancer diagnosis, and thus the FFQ is capturing diet modifications caused by the disease. Sensitivity analyses excluding advanced stage cancers could clarify this.

12. The authors note that the potential misclassification of exposure in their data is non-differential. This is debatable since the dietary information among cases was collected after cancer diagnosis (and the disease diagnosis may have influenced their recall), and EAC and EGJAC cases were more likely to be obese (there is abundant literature showing that obese individuals are more likely to substantially underreport their dietary intakes). The authors should acknowledge a potential for differential misclassification of exposure in their study and discuss it in more detail.

Minor Essential Revisions

13. The ICD codes were not included.

**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.