Reviewer’s report

Title: Macronutrients, vitamins and minerals intake and risk of esophageal squamous cell carcinoma: a case-control study in Iran

Version: 4 Date: 15 September 2011

Reviewer: Meira Epplien

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Major comments:

1. The presentation of the case-control difference in percent complied with international nutrient guidelines does not add to this paper. This is especially true in light of the authors’ own admission that the use of a semi-quantitative FFQ “is well-recognized for its weakness in quantification of nutrient intakes” (p. 19). I would remove the figures, and merely add a line or two in the discussion section (or introduction section) to note the general non-compliance with these guidelines among this population. If the authors would like to draw attention to this issue, I suggest a separate paper that would include multivariate ORs (as performed in Tables 1 and 2).

2. Because, as the authors correctly note, the numbers are very small in individual cells in these analyses, n’s should be included in Tables 1 and 2, so that the readers can see the number of cases that contributed to the ORs for each tertile. I realize that these tables are already very large, so I suggest that the means and standard deviations, and cut-off points as presented in the footnotes, be removed to supplemental materials.

3. Even after re-reading the methods section, I am confused as to the selection and categorization of potential confounders. Specifically:

   a) I do not see how this study has the power to adjust for NSAIDs use, as none of the controls (as presented in Table 1) were identified as NSAIDs users.

   b) Education level was categorized as <5 vs. #5 years, and yet only 4 controls, and no cases, reported #5 years of education (see Table 1). It appears that a more reasonable categorization would be illiterate vs. #1 year of education.

   c) While the limitation of categorizing a continuous variable, such as age, is mentioned in the discussion section, it is still not explained why this variable was categorized. I would prefer to see it modeled as a continuous variable, unless there is a reasonable explanation of why that is not a good idea.

4. The discussion section includes too many explanations of biological mechanisms that are not specifically pertinent to the present study. Most of these descriptions are of the general potential carcinogenic (or anti-carcinogenic) effect of various nutrients. More salient would be the mechanisms that are specific to
ESCC – listing possible mechanisms for incidence of any cancer does not add to the discussion, and contributes to the excessive length of this section.

Minor comments:

1. In the methods section, p. 6, it is reported that previous studies have reported “good correlations between dietary intakes assessed by the FFQ and those obtained from 24-h dietary recalls.” Please report the relevant correlations here.

2. The results section is much too wordy, primarily due to the repetition of the reporting of specific results already presented in the tables. I would remove specific numbers (such as average intakes as presented on p. 10) and instead state the fact (e.g., “Cases consumed significantly more SFA and discretionary calories compared to controls.”) and refer the reader to the appropriate table.

3. The results of the joint effects of vitamin E and folate (Table 4) should be presented more clearly so to be easier for the reader to assess. Specifically:
   a) only report ORs and CIs to two decimal points
   b) show the sample size (n) for each cell
   c) present the P for interaction

4. If it is thought that the effect of a high fat diet might be mediated by BMI (p. 13), it would also be worthwhile to examine the possibility of effect modification by BMI.

5. It is noted in the discussion (p. 14) that the association of a protective effect of high consumption of carbohydrates might be due to its association with lower intake of fat and/or high intake of fruits and vegetables. To add to this discussion, these variables should be put in the same model and the results reported, or at the least the actual correlations between these variables in this population should be reported.

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.