Reviewer's report

Title: Family history of cancer, personal history of medical conditions and risk of oral cavity cancer in France: the ICARE study.

Version: 1 Date: 25 June 2013

Reviewer: Linda Morris Brown

Reviewer's report:

- Major Compulsory Revisions
  1) Authors need to address the potential issue of multicollinearity in their logistic regression models that may have resulted from inclusion of 3 smoking variables, all with the same reference category of “Never smokers”.
  2) Authors need to explain why they looked at head and neck cancer among relatives instead of just oral cancer and specifically why nasal cavity and sinuses were included. Other studies have looked at UADT cancers in relatives (oral cavity, pharynx, larynx, and esophagus).
  3) Authors should explain their rationale for the second set of model adjustments in Table 2 since most of these additional variables don’t appear to be related to risk of oral cancer and risk of each other. Suggestion is to remove this additional adjustment.
  4) Authors should put in the text the actual questions used to collect the information on family history and personal medical conditions (especially oral candidiasis).
  5) Is there any additional information available on oral candidiasis such as interval between diagnosis and oral cancer that would help determine whether this was related to pre-oral cancer vs an early consequence of disease?
  6) The authors need to include the possibility of uncontrolled confounding as a possible limitation. They comment in the discussion that the large number of subjects in each category allowed for satisfactory adjustment, but this may not be true for some of the risk factors of interest where the number of cases with condition (oral candidiasis) or a family member with cancer may be small.

- Minor Essential Revisions
  1) The authors should simplify the introduction and move much of the discussion of the results of past studies to the discussion.
  2) In the introduction, should talk about the specific analysis planned instead of what was done for the larger ICARE study. For example (first paragraph page 4). In order to explore the role of family history of cancer and personal medical history in the etiology of oral cancer in France, we used data from the ICARE study (…). An explanation of the ICARE study can remain in the methods.
  3) Suggest removing Table 6 and putting relevant information in the text
4) Table 5 should footnote the reference categories.

5) The explanation of Table 5 in the text is confusing. It would probably be better to note that significantly elevated risks of oral cancer with family history of head and neck cancer were seen for both never and ever smokers and for light and moderate to heavy drinkers. However, the risk was small and not significant for NS and D< 2 suggesting some association with drinking or smoking.

- Discretionary Revisions

1) Many studies have found a stronger relationship with family history among younger compared to older subjects. The authors may want to review the literature and add to the discussion if appropriate.

2) Authors may want to review article on oral candidiasis by Sanjaya PR, et al in Med Hyotheses 77(6) 1125-8, 2011 and add to the discussion if appropriate.

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

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests