Author's response to reviews

Title: Reproductive factors and oesophageal cancer in Chinese women: a case-control study

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Version: 3 Date: 13 April 2011

Author's response to reviews: see over
Dear Editor,

We are pleased to have received your email dated April 11, 2011, in which we were encouraged to submit a revision of the manuscript entitled “Reproductive factors and oesophageal cancer in Chinese women: a case-control study” we submitted to BMC Gastroenterol. We have addressed all the concerns of reviewers according to the reviewers’ suggestions.

On the following pages, please find our point-by-point responses to the reviewers.

We wish to thank you and three reviewers for many constructive comments and suggestions that have greatly enhanced the quality of the manuscript. We hope the concerns have been addressed adequately in this revision.

Sincerely,

Zu-Hui Chen, Jian-Li Shao, Jin-Rong Lin, Xia Zhang, Qing Chen
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Response to reviewers’ comments on the manuscript entitled "Reproductive factors and oesophageal cancer in Chinese women: a case-control study" submitted by Chen et al to BMC Gastroenterol for publication

Reviewer: Ian Beales

Major compulsory revisions

1. I do not understand how the authors claim that the risk of esophageal cancer is inversely related to age at first birth? Pages 3 and 9. The risk appears to increase with age at first birth. If the risk were inversely related to age at first birth would not the OR be lower for the those mothers giving birth later in life?

Response: Thanks for carefully reading our manuscript and pointing out the error. We have replaced these statements with “The risk of oesophageal cancer increased with age at first birth” in the revised manuscript.

2. Was any effort made to correct for the consumption of potential confounding factors particularly aspirin and NSAID use? It may be that these factors are not prevalent in this population but even if this is the case, the manuscript should cover this.

Response: Thanks for the comment. We have added the statements “Potential confounders entered into the final model included: age, reflux, smoking, alcohol use, education, employment, body mass index, and intake of fresh vegetables and fruits. We also considered further adjustment for aspirin or nonsteroidal anti-inflammatory drugs (NSAID) use but the estimated ORs did not substantially changed. Also because only a very small proportion of the subjects (lower than 10% for both cases and controls) had regular use of such medicines, aspirin or NSAID use was not included in the final models.” into the statistical analysis part in the method section.

3. Although I do think the overall paper would be improved by actually including the data for squamous and adenocarcinomas separately as well as pooled. The authors do mention briefly, some subgroup analysis but I do feel that at the very least the OR
for birth age (the main significant finding of this study) should be provided separately for both histological types of cancer. These data can be provided within the text of the results section. Even if not statistically significant, it would be useful to include these.

**Discretionary Revisions**

4. I would recommend including tables on squamous and adenocarcinomas separately as well as the pooled data.

**Response:** Thanks for the suggestions. We present results for squamous cell oesophageal cancer and all histological types separately in table 2. However, because there were only 5 adenocarcinoma cases, we did not present results for adenocarcinoma in the revised manuscript.
Reviewer: Neal D Freedman

Minor Essential Revisions:

1. Please add the results for age at menopause to the abstract and to the results section (top of page 9).

Response: Thanks for the suggestion. We have added these results to the abstract and the results section according to the reviewer’s suggestion.


Response: We have updated the information using GLOBACAN 2008 in the revised manuscript.

3. The authors mention that the male/female ratio is up to 8:1 in Western countries; yet somewhat lower in Asian countries. According to globalcan 2008, the overall sex ratio for esophageal cancer is about 2 in China. Thus, the authors’ statement is misleading.

Response: Thanks for the valuable comments. We have revised the manuscript according to the reviewer’s comment. Particularly, we have added the statements “The male to female ratio of oesophageal cancer incidence rates is much lower in Asian countries. In 2008, the male to female ratio of oesophageal cancer incidence rates was about 2 in China” into the background section.

4. On the top of page 5, the authors mention that “tobacco smoking plays only a moderate role as a risk factor for this cancer.” This statement is false. Smoking is a strong cause of esophageal squamous cell carcinoma and is a consistent risk factor for esophageal adenocarcinoma as well. In most western populations, men and smoke similar amounts. Thus, in Western populations, differences in smoking use between men and women are not likely to cause higher rates of esophageal cancer in men. In China, however, men tend to smoke more cigarettes and drink more alcoholic beverages than women. It is possible that these differences in cigarette smoking and alcohol drinking may explain part of the difference in esophageal cancer incidence
rates in men and women in China. The authors should mention these points.

**Response**: Thanks very much for the comment. We have revised the manuscript according to the reviewer’s comment. Particularly, we have added the statements “*It is possible that differences in extrinsic exposures, such as cigarette smoking and alcohol drinking, may explain part of the difference in esophageal cancer incidence rates in men and women in China*” into the background section.

5. The authors should clearly indicate in their introduction that while several studies have investigated the association of menstrual and reproductive factors with esophageal adenocarcinoma, few studies have examined associations with esophageal squamous cell carcinoma. As currently written, this section implies that esophageal adenocarcinoma in Western countries is comparable to esophageal squamous cell carcinoma in China, it is not.

**Response**: Thanks for the valuable comment. We have added the statements “*In addition, squamous cell oesophageal cancer represents the majority of oesophageal cancer cases in China. Thus, previous evidences from western countries mostly concerning the effect of reproductive factors on the risk of oesophageal adenocarcinoma may not apply to Chinese populations*” into the background section in the revised manuscript.


**Response**: Thanks for carefully reading our manuscript. We have corrected this typing error.