Author's response to reviews

Title: Estimation of cancer incidence and mortality attributable to alcohol drinking in China

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Author's response to reviews: see over
Dear Dr. Roxane Rajabi,

Thank you very much for your letter dated September 23 and for the accompanying reviewers’ comments on our paper (9740505714254879). We are submitting a revised manuscript that incorporates the comments of the reviewers. A point-by-point response to 2 of the reviewers’ comments is attached as follows.

For your kindly comments on revising the paper to make it adhere to the PRISMA guidelines, we think our study is not a systematic review, because we did not conduct a meta-analysis by ourselves. We merely picked appropriate studies from our literature review that met our criteria to apply in our study to calculate the PAF in China. Other similar studies “Estimation of cancer incidence and mortality attributable to smoking in China” have been published in Cancer Causes Control (2010) 21:959-965. All the data on our study is openly available. Please let me know if our study should still be considered a meta-analysis and we will revise to meet the PRISMA guidelines.

We hope that our paper has been revised satisfactorily and will be accepted for publication in BMC Public Health.

We look forward to your response.

Sincerely,
Youlin Qiao    M.D. Ph.D.
Hao Liang    M.D.

Attachment:  Point-by-point response to the reviewer’s comments received on 9/23/2010

Associate Editor's comments:
The authors need to consider in a greater detail possible bias that could have occurred in their research (i.e., omitted variable bias, information and selection bias).

Response: We have rephrased the paper and added some biases in the discussion: “some biases need to be considered: such as that data on cancer incidence were not available and were estimated based on mortality to incidence ratios, which may be subject to bias; also, meta-analyses applied in our study were obtained from case-control studies which are generally considered more susceptible to recall and selection biases than cohort studies”

Reviewer #1:
Comment #1.1: Abstract-methods: describe as meta-analyses and studies searches were conducted.
Response 1.1: Actually, our paper is not a meta-analysis. Our methods were to estimate the proportion of cancer deaths and cases in China in 2005 attributable to alcohol drinking, based on data of exposure around 1990.

Comment #1.2:
In Methods(text) when you say "A systematic literature review of studies on alcohol and cancer was
Comment: We think our study is not a traditional systematic review, so we just chose the appropriate questions to answer as follows. Others are not appropriate for our study.

#1.21 - types of search on database: eg. keyword on databases (PubMed, Ovid, CNKI, etc) for outcomes studies

Response 1.21: We have rephrased the sentences: “Data on RR of alcohol and cancer was conducted through a search from 1990 to 2008, in the databases PubMed, Ovid, China National Knowledge Infrastructure (CNKI), VIP Information and authoritative publications or data from Ministry of Health in China”. The searching words involve “meta-analysis”, “case-control study”, “cohort study”, “alcohol drinking”, “alcohol consumption”, “China” and the names of specific cancers.

#1.22-restriction (exclusion/criteria)for studies outcome(eg. English-language articles restriction ..)and definition “The research was concluded on ../../...”

Response 1.22: We have rephrase the sentences: “Inclusion criteria of studies were: 1) Obtained in recent 10 years; 2) Contain relative risk or odds ratio and corresponding 95% confidence intervals; 3) Meta-analysis or large-scale surveys of representative samples of China were given the highest priority, followed by non-representative samples of China, or meta-analysis from Asian or western countries. 4) Definition of RRs of alcohol drinking and cancers is consistent with our study”.

#1.23-Data extraction: missing methodology for data extraction

Response 1.23: Not appropriate

#1.24- Data synthesis:

eg. "A total of n. studies found through PubMed, Ovid, ..etc and n. studies met our inclusion criteria"

Response 1.24: Actually, we picked the most appropriate studies which have been listed in our paper when doing the literature review, rather than including every single paper which met our search criteria.

#1.25- Missing data: "Meta-analysis / statistical analysis was performed using .... software...."

Response 1.25: Not appropriate

Reviewer #2:

Comment #2.1: Methods, 5th line: In your study most of the cancers causally associated with alcohol drinking are taken into consideration “(…) oral cavity, larynx, pharynx, esophagus, liver, female breast as well as colorectum”, except that pancreas cancer. I think that also data about pancreas cancer should be analyzed, since it’s strongly related with alcohol consumption.

Response 2.1: We have added these into the discussion part to explain why we didn’t take into account pancreatic cancer. Actually, alcohol-related cancer has been greatly evaluated by the cited reference: “World Cancer Research Fund / American Institute for Cancer Research. Food, Nutrition, Physical Activity, and the Prevention of Cancer: a Global Perspective” which has conducted a comprehensive systematic review worldwide and showed that the evidence between pancreatic cancer and alcohol drinking is too limited to permit a probable or convincing causal
judgment. Also, we have reviewed Chinese literature, and “A Meta analyses of risk factors for pancreatic cancer in China” with 1889 cases and 10304 controls reported no association of pancreatic cancer with alcohol. In other studies which showed positive results, we think residual confounding cannot be ruled out since tobacco smoking is a strong risk factor for pancreatic cancer. The available evidence for an association between pancreatic cancer and alcohol consumption is not convincing.

Comment #2.2: Methods, 2th paragraph: In your study you define alcohol consumption as “drinking alcohol on at least 12 occasions during the past 12 months”, moreover you do not take in account neither the type of alcohol nor the drinking patterns: in my opinion this is a questionable parameter; this parameter is not selective since most of the population all over the world could be considered an alcohol drinker according to this standard, and, in this way it would lead to an overestimate of the effect of alcohol.
Response 2.2: We agree with the reviewer that it may lead to an overestimate. We have added this comment into our discussion. But we have to use this definition (drink or not drink during the past 12 months) due to a lack of Chinese data on quantitative analysis for alcohol drinking and specific cancers.

Comment #2.3: Discussion, 55th line: In your paper you affirm: “With respect to head and neck cancers (oral cavity, pharynx, and larynx), although there is strong evidence of a causal association with alcohol drinking, the low incidence of these cancers in China resulted in a relatively small number of cancers attributable to alcohol”: why do you think it could be possible? Maybe other risk factors (probably linked to the Chinese culture and traditions) are involved in the pathogenesis of these kind of cancers? Please give elucidations.
Response 2.3:
The number of cancers attributable to alcohol=PAF*Number of Cancer motility/incidence
Sorry if we were unclear, we mean that although the PAF for head and neck cancers is high (34%) compared to other cancers, head and neck cancers in general are rare in China according to the national cancer death survey data, so the numbers of total number of cancers attributable to alcohol is low. Other risk factors for head and neck cancers include smoking (PAF=24.6%), infection, and low fruit and vegetable intake. (We are not sure if we will add these sentences to the paper)

Comment #2.4: Discussion, 59th line: You state that “Our results have several limitations”. Your limits lead to an important overestimation of the role of alcohol in the cancers pathogenesis: is it possible to modify some parameter in order to reduce the overestimation?
Response 2.4: According to the formula, the PAF is related to 2 parameters: risk factor (RR or OR) and prevalence of exposure (P); P is fixed due to national surveys in China. RR we obtained from meta-analyses or large-scale surveys of representative samples of China has also fixed, which can not solve the problems of bias and confounding, we will recognize the limit in our paper.

Comment #2.5: Discussion, 80th line: Your discussion ends with the affirmation “(…) low and
moderate (1-2 drinks/day) alcohol consumption might reduce the risk of cardiovascular disease. Particular attention needs to be paid regarding the potential harms of alcohol as well as its potential benefits when making public health recommendations on alcohol drinking and cancer surveillance”. Which are your own recommendations about this problem? Since you state that 12 drinks/year could cause a cancer, it would better to explain to the reader how you think it would be better to behave regarding alcohol consumption, not only recommending “…particular attention…”.

Response 2.5: We have rephrased the sentence, although in our conclusion that 12 drinks/year could cause cancer, the important factor is the amount of ethanol consumed, and we give the example of recommendations for Dietary Guidelines for Chinese Residents.