Author's response to reviews

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

Authors:

Hao Liang (lianghaopumc@gmail.com)
Jian-Bing Wang (wangjianbing1980@yahoo.com)
Hui-Juan Xiao (xhi60000@163.com)
Ding Wang (wendyding@126.com)
Wen-Qiang Wei (weiwg@cicams.ac.cn)
Paolo Boffetta (paolo.boffetta@i-pri.org)
You-Lin Qiao (qiaoy@cicams.ac.cn)

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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 or meta-analyses. We merely picked appropriate studies from our literature review that met our criteria to apply in our study to calculate the PAF. Our purpose is to estimate the contribution of alcohol drinking to the burden of cancer mortality and incidence in China in 2005. All the data on our study is openly available. 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 in discussion part: “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. However, most attributable cases were from lethal cancers, and the extrapolation from mortality data was not a great issue. 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; misclassification of past alcohol drinking may lead to an observation bias”

Reviewer #1:
Comment #1.1: Abstract-methods: describe as meta-analyses and studies searches were conducted.
Response 1.1: We are afraid that we may not revise methods as meta-analyses, because we did not conduct Meta-analyses by ourselves. We picked Meta-analysis or large-scale studies from the literature review that met our criteria to apply in our study to calculate the PAF in China. Our methods are to estimate the contribution of alcohol drinking to the specific cancer burden in China in 2005, based on frequency of exposure around 1990.

Comment #1.2:
In Methods(text) when you say "A systematic literature review of studies on alcohol and cancer was
conducted..." additional necessary descriptions are specify
Response: We may not express clear. We did not conduct a systematic literature review in our study, we use the data from published systematic literature reviews. We have deleted the sentences related to the word of “systematic review”.
#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 and added in “Data used for estimating relative risk (RR) of alcohol drinking and cancers” part: “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 rephrased 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–related cancers was consistent with our study”.
#1.23-Data extraction: missing methodology for data extraction
Response 1.23:
We did not conduct a meta-analysis, and have added the sentence (see “Data used for estimating relative risk (RR) of alcohol drinking and cancers” part): “For each study, we extracted details on study design, population, number of subjects (cases, controls or cohort size), sex of the population considered, confounders allowed for in the analysis, RR estimates for categories of alcohol consumption and the corresponding 95% CI”.

#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: We did not conduct a meta-analysis, we use SAS software to calculate the PAF and alcohol-related cancer burden.

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 agree with the reviewer and find some study shows strong association between alcohol drinking and pancreatic cancer, and we have added these into the discussion part, try 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 limit 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 into 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: Actually in China, we only have 2 national surveys refers to alcohol drinking (in 1991 and 2002) which can represent Chinese population, the definition of alcohol drinking is at least 12 occasions during the past 12 months, without consideration of drinking patterns and alcohol type. We have discussed it in the discussion section (see limitation from discussion part).

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 kinds of cancers? Please give elucidations.

Response 2.3: We try to explain that The number of cancers attributable to alcohol=PAF*Number of Cancer motility/incidence, 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.

We have added the elucidation:” Other major risk factor for these cancers including tobacco smoking, HPV infection and dietary factors, such as low fruit and vegetable intake has been well established. Also, previous study has reported 24.6% of head and neck cancers could
attributable to smoking.”

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: In the discussion part, some of the original studies included in the meta-analyses may not have adjusted the risk estimates for alcohol for potential confounding factors, such as smoking for head and neck cancer, or HBV and HCV infection for liver cancer, leading to an overestimate. However, It should be stressed that we chosen the good quality of meta-analysis of Chinese studies for the RR estimate. We have to admit the limitation in our study and it may not be possible to reduce the overestimation. Other overestimation, referred to definition of alcohol, see comments and response #2.2.

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 alcohol drinking 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 (see the end of paragraph).