Author's response to reviews

Title: Role of Verbal Autopsy in determining high occurrence of cancer along Huai River Basin, in China

Authors:

Xia Wan Dr. (wanxia.china@gmail.com)
Maigeng Zhou Dr. (maigengzhou@126.com)
Zhuang Tao Dr. (chijingba@vip.sina.com)
Gonghuan Yang Prof. (yangghuan@vip.sina.com)

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

Thank you for your time and suggestions for improving our manuscript.

The current study is part of a large study on the relationship between water pollutions of the Huai River and cancers. We have examined numerous risk factors in the larger study but could not include all information in the previous draft due to words limit. Your critiques on our previous draft are helpful and the additional information you requested is critical. We have addressed your questions and concerns in the current draft. Please find point-to-point response (in Italics) as follows.

1. We need to know more about the differences in cancer risk between the study and control areas. GDP, but also diet, sanitation, smoking, alcohol, salt, anything that might affect cancer risk. If we understand what are the likely differences in exposure between control and study counties/districts, we will be better able to interpret the results. Please include a detailed discussion in the Discussion section.

   We appreciate this suggestion. In fact, during our prior investigation, we examined other risk factors of cancer, such as infections with Helicobacter pylori and Hepatitis B, smoking, alcohol use, dietary behavior (e.g., consuming pickled, smoked food), and indoor cooking and heating practices, and education level, income and health care. However, we did not find any significant differences in these factors between the study and control areas. We now have included several sentences in Discussion to address this point.

2. Why are the death and prevalence rates from cancer so LOW in the control areas? Are they better educated? Were the VA procedures done better/worse there? How do these rates (age standardized) compare to other parts of China? Are these low rates consistent with the prevalence of risk factors?

   Based on the 1973-1975 Survey, both counties had low prevalence rates of cancer (only around 70% of the national prevalence for rural areas). During the current investigation, we found that cancer prevalence rates in the control areas in the same counties remained low (60-65% of the national prevalence for rural areas). Therefore, cancer prevalence rates in the study and control areas have been low until the recent rise in the study areas where villagers relied on polluted water sources for drinking water.

   VA procedures have been conducted similarly in the study and control areas. We have been making efforts not to impose biases during the VA process.

3. Are the prevalence rates seriously biased by the fact that only about 50% of cancer patients attend health facilities before death? There is a clear underreporting of prevalence. Is this underreporting likely to be higher in control vs study areas? If so, why and how will this affect your comparisons?

   We apologize for the confusion caused by our previous wording. In the previous draft, what we meant to present was that only around 50% of all deceased population (n=3301) had visited health facilities before death. In fact, among the 1158 deaths caused by cancers, around 84% had visited a health facility before death. Because the thesis of the current study was using VA for cancer diagnosis, we decided to report health facility utility rates for cancer-related deaths (See Results).

   We understand that missing cases is inevitable in most studies. Therefore, we have adopted strict quality control procedures to minimize underreporting (see Methods and Discussion). There is no evidence for differential underreporting between the study and control areas.
4. We need more detail on EXACTLY what VA questionnaire was used, what training the physician reviewers had to diagnose cause of death, and what percentage of cases went to third review. Please give as much detail as possible on the VA procedure and include a copy of the VA form in an Appendix.

The physician reviewers had completed a training course on how to use VA questionnaire for cancer diagnoses. A total of 11.67% of cases went to a third review. We have added additional sentences to provide more details per editor’s request in the Methods section of the paper.

Complete questions of the VA questionnaire can be found in references we provided, such as verbal autopsy standards\(^2\) and validation of verbal autopsy procedures for adult deaths in China.\(^3\)

References:

Please do not hesitate to contact us for further questions.

Thank you very much!

Best regards,
Gonghuan Yang