

Peer Review File

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Review Comments

Reviewer A

Comment 1: The rationale of the study is unclear. The authors stated at the end of the introduction that the objective is "to provide ideas for cancer prevention, screening, diagnosis and treatment of cancers in China". However, such an objective is not achieved by a comparison of cancer incidence and mortality rate. Instead, the authors should qualitatively and quantitatively examine the differences in the primary, secondary and tertiary cancer interventions, such as the prevalence of risk factors, the availability and uptake of screening programs, the utilization of health care facilities for cancer diagnosis and treatment, etc.

Reply 1: Thank you for this suggestion. We believe that statistics on incidence and mortality are the basic and fundamental work of cancer research. How a country or region specifically develops cancer risk factor prevention, cancer screening, or other intervention work needs to be based on the characteristics of cancer incidence and death. Therefore, we believe that by comparing the incidence and mortality of cancer between the two countries, and analyzing the achievements of the two countries' cancer prevention and control work, it will help to achieve the objective of this article. We have made a new description of the content you mentioned in the discussion section. Please check it out.

Changes in the text: We have modified our text as advised (see Page 5, line 1 to Page 7, line 2)

Comment 2: Notwithstanding my concern on the rationale of the study, I wonder why the authors only compared China to USA. It is well-known that USA does not perform the best in terms of cancer registry, cancer prevention, or cancer survival. For example, USA did not even participate in the International Cancer Benchmarking Partnership. Wouldn't it be more informative, if the authors include more countries, both developed and developing, to see where China stands? With respect to the

comparison, the authors calculated incidence and mortality rate ratios, but did not provide confidence intervals.

Reply 2: Thank you for the kind comment. As you said, the United States might not be the best country in the world for cancer prevention and treatment, but the purpose of this article is not to compare or learn how different countries carry out cancer registration. The United States may be the country with the most open and accessible cancer data. The United States publishes the Cancer Statistics and other cancer prevention and control related publications every year, and its influence is also powerful. According to the trend of cancer incidence and mortality in the United States, the impact of its prevention and treatment measures can be specifically seen.

We also thank you for the suggestion to include more developed countries and developing countries for comparison. Due to the limited length of this article, we are very willing to take your valuable advice in the design of our next study.

Regarding the question of providing confidence intervals, our research is a secondary analysis of the global cancer statistics 2020, and we hope but may not be able to provide confidence intervals for the ratios. Thank you.

Changes in the text: We have modified our text as advised (see Page 5, line 6 to 20)

Comment 3: The writing needs improvement. Please consider inviting a native speaker to proofread the manuscript. There are numerous grammatical errors and poor use of English throughout the article. Below are several examples:

- In many places including the title, article "the" is missing from "the United States". And in several places, it was spelled as "the Unite States".
- Page 4 line 13, "cancer new cases" should be "new cancer cases".
- Page 4 line 22, "we attempts" should be either "we attempt" or "we attempted".
- The abbreviation of age-standardized incidence rates is ASIR, not ASMIW (likewise for age-standardized mortality rate).
- Page 10 line 5, "The accumulating damage of bad lifestyle habits on cancer". Did the author mean that bad lifestyle habits cause damage on cancer?
- Page 10 line 8, "Doing a good job in the primary prevention ..." is acceptable as spoken language, but not in a scientific paper.
- Page 12 line 12, "China is still relatively backward in the ...". "backward" means going in the opposite direction. Here "lagging behind" should be used.

- Page 13 line 3, what is "double burden of cancer"?

Reply 3: We sincerely thank you for careful reading. We have polished the language of the article and changed the part you mentioned accordingly. The revised contents were highlighted in blue colors in the revised manuscript. Great thanks!

Changes in the text: Page 8 Line 7; Page 6 Line 21; Page 9 Line 2; Page 13 Line 11; Page 13 Line 13; Page 16 Line 19.

Comment 4: Besides the major issues, here are a few minor issues:

- 1). I'm not sure what purpose does the first paragraph of the introduction serve. Quite pointless and can be completely removed in my opinion.
- 2). On page 5 line 3 and page 13 line 16, the authors stated that they have completed the STROBE checklist. Although it was not attached with the manuscript, I would be very interested in how they managed to fill a checklist that is irrelevant to the presented study.
- 3). The format of reference is inconsistent.

Reply 4: 1) We have rewritten the introduction section, please check.

2) The STROBE checklist was uploaded in the submission system.

3) We have revised the format of references.

Thank you for careful reading.

Changes in the text: Introduction; Reference.

Reviewer B

Comment 1: English language of the paper is still problematic, which needs further editing after revisions.

Reply 1: We sincerely thank you for careful reading. We have polished the language of the article. Please see the revision in our manuscript.

Comment 2: The title did not fully reflect the research work done by the authors, descriptions and comparisons of cancer burden between China and the US. Please consider revising it. The term "burden" is not accurate. Does it refer to disease burden?

Reply 2: Thank you for the kind comment. We changed the title to "Comparison of cancer incidence and mortality between China and the United States".

Changes in the text: Title

Comment 3: Abstract. In the part of method, please specify the standard population and how these indicators of burden were standardized. The authors may consider providing a little more details of the data source. In the part of results, I think standardized incidence rates are important, in addition to ratios of the two countries. Please also provide the absolute numbers of persons with cancers. This is also an important indicator of disease burden. The conclusion part needs further insights on the clinical implications, for example, country- and cancer-specific prevention strategies for China and the US. Further, the authors should not only repeat the main findings. It is necessary to briefly mention the underlying reasons for such differences.

Reply 3: Thanks for your kindly suggestion. Here is the revised new Abstract.

“Background: To summarize and compare the difference of cancer incidence and mortality between China and the US.

Methods: Incidence and mortality data were extracted from the GLOBOCAN2020. US data were obtained from the American Cancer Society, while China’s data were obtained from 92 cancer registries in rural and urban settings. Age-standardized incidence or mortality rates were presented based on the World Standard Population which proposed by Segi (1960). Incidence rate ratio and mortality rate ratio were calculated to compare the difference between the two countries.

Results: In 2020, there are 4.6 million and 2.3 million 19.3 million new cases for in China and the US, respectively. The age-standardized incidence rates of all cancers in China and the US are 174.0 per 100,000 and 318.0 per 100,000, respectively. The incidence rate ratio of all cancer China to the US is 0.57, while the mortality rate ratio is 1.50. The age-standardized incidence rates of melanoma, prostate cancer, and hodgkin's lymphoma in US are 46.1 times, 7.1 times and 5.4 times greater in China, respectively. While the age-standardized incidence rates of nasopharynx cancer, oesophagus cancer and stomach cancer in China are 7.5 times, 4.9 times and 4.9 times that of the US, respectively. The age-standardized mortality rates of nasopharynx cancer, oesophagus cancer and stomach cancer are 10.0 times, 5.3 times and 9.4 times that of the US, respectively. The age-standardized mortality rates of oropharynx cancer, testis cancer, corpus uteri cancer, vulva cancer, mesothelioma, multiple

myeloma and melanoma of skin in the US are 2.5 to 6.1 times greater in China.

Conclusions: There are big differences in the cancer spectrum between the two countries. Factors of economy, environment, diet and living habits are the possible reasons for such differences. While facing increasing tumor burden challenge, improving residents' awareness of risk factors, recognizing genetic risk and strengthening early screening are feasible options to be implemented.”

Hope these modifications can meet your requirements.

Changes in the text: Abstract

Comment 4: Introduction. This part is inadequate. The authors did not clarify why a China-US comparison in burden of cancer deserves to be studied. The authors may consider the different socio-economic-cultural, lifestyles, dietary, and healthcare system to indicate the difference in patterns of cancer, which may be related to the different burden of cancer. Macro-level risk factors of cancer are needed to be reviewed here. The second point is the public health and clinical significance of results from such comparisons. The authors need to provide their insights. Third, indicators of burden of cancer need to be defined here, for example, why not directly consider disease burden such as DALY and PYLL. Fourth, please have some reviews on the history, current status, progress, and quality of the cancer-related vital surveillance systems of China and US, since quality data are necessary for the comparison.

Reply 4: Thank you for your questions. The first point, although China has achieved significant results in economic development, there is still a clear gap between China and the US in the medical and health care. The incidence and mortality profiles of China are changing from those of developing countries to those of developed countries. Even the mortality rate of many cancers in China is higher than that in the US. Obviously, China needs to establish and refine a cancer control system at the state level to suit current socioeconomic status. There are striking geographic differences in the incidence and mortality of different cancer types in different world regions. This diversity reflects both the presence of local risk factors for specific cancers, and the extent to which effective cancer control measures have been implemented. The cancer mortality rate in the US continued to decline from its peak in 1991 to 2018, and the total mortality rate fell by 31%. Among them, it fell by 2.4% from 2017 to 2018,

which was a record-breaking decline for the second consecutive year. Therefore, the experience and results of cancer prevention and treatment in the US are worth learning from all over the world. The second point, the aim of our study is to provide possible directions for cancer prevention, screening, and control in China. For example, education on the prevention of cancer of the digestive system need to be strengthened. Enhance residents' awareness of possible risks. Provide residents with comprehensive early screening and treatment approach, etc. The third point, this is the limitation of our study. Other indicators of burden of cancer such as DAILY and PYLL need to be analyzed in future studies. The fourth point. Since China's first cancer registry was established and operated in Linzhou in 1959, China has established a total of 574 cancer registries by 2019, covering a population of 438 million (31.5% of the Chinese population). Of this population, 48% were covered by urban cancer registries and 52% by rural cancer registries. Each year, the National Central Cancer Registry, acting as the national bureau for the management of cancer registration, conducts cancer registration training programmes and is responsible for the collection, management, and analysis of nationwide cancer registry data. In addition, China has also issued regulations on the management of cancer registration, providing sustainable funds to promote the continuous improvement of cancer registration in China. The US Cancer Statistics are the official federal cancer statistics. These statistics include cancer registry data from CDC's National Program of Cancer Registries (NPCR) and the National Cancer Institute's (NCI) Surveillance, Epidemiology, and End Results (SEER) Program, as well as mortality data from CDC's National Center for Health Statistics. The CDC-funded NPCR is established in 1992 and The NCI-funded SEER Program was established in 1973. Today, the NPCR supports central cancer registries in 45 states, the District of Columbia, Puerto Rico, and the US Pacific Island Jurisdictions. The data represent 96% of the US population. SEER collects and publishes cancer incidence and survival data from population-based cancer registries in 19 US geographic areas, which represent 48% of the US population.

Changes in the text: Introduction

Comment 5: Methodology. The data sources of the two countries should be describe in detail. The authors need to describe the quality control measures of the two

mortality surveillance systems and indicate whether adjusting for underreporting is necessary.

Reply 5: Thank you for your suggestions. Incidence data are produced by population-based cancer registries (PBCR). Mortality statistics are collected and made available by the WHO. US data are from national sources (CDC's National Program of Cancer Registries, NIH's Surveillance, Epidemiology, and End Results). China's data are from local sources (92 cancer registries in rural and urban settings). The quality control measures of the two mortality surveillance systems are described online at the Global Cancer Observatory (GCO) (gco.iarc.fr). Since we do not collect original data, the corresponding content can be consulted through the original literature, and we have listed references in the corresponding section.

Changes in the text: We have modified our text as advised (see Page 7, line 4 to Page 8, line 4)

Comment 6: Statistics. Please define prevalence, incidence, and mortality here. I do not think the current version of statistics is adequate. Please specify the procedure of standardization; otherwise the comparison results are problematic. For comparisons, I do not think ratio is a good measure to indicate the difference in cancer burden. Please consider prevalence ratio and incidence rate ratio and their 95% CIs.

Reply 6: Cancer incidence is the number of new cancer cases arising in a specified period and geographic area, conveyed either as an absolute number of cases per annum or as a rate per 100,000 persons per year. Similarly, cancer mortality is the number of deaths occurring in a specified region and period, and the mortality rate is the number of deaths per 100,000 persons per year. We present age-standardized incidence or mortality rates (ASR) per 100,000 person-years based on the 1966 Segi-Doll World standard population. We believe that statistics on incidence and mortality are the basic and fundamental work of cancer research. Prevalence and its ratio are also important indicators. However, due to the limited length of this article and table, we are very willing to take your valuable advice into consideration in the next study. Incidence rate ratio is provided in the manuscript. We may not be able to provide confidence intervals for the ratios since our research is a secondary analysis.

Changes in the text: We have modified our text as advised (see Page 8, line 6 to Page 8, line 16)

Comment 7: Discussion. Please also consider population aging, genetic, dietary, rural-urban, and geographic difference when explaining the findings.

Reply 7: Thank you for your kindly suggestions. **Population aging** is the third paragraph of the discussion. Genetic factors are discussed in **Early screening**. Dietary factors are discussed in **Preventable carcinogenic risk factors**. Geographical location itself cannot be the cause of cancer. The hidden economic and environmental differences behind the geographic location are the real reasons of the differences in cancer incidence and mortality. **Economic and environmental factors** are added.

Changes in the text: Discussion