Author’s response to reviews

Title: Cost of illness of the Stomach Cancer in Japan - a time trend and future projections -

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Author’s response to reviews: see over
Dear Dr. Joses Muthuri Kirigia

We are grateful to Dr. Kirigia (reviewer 2) for the critical comments and useful suggestions that have helped us to improve our paper. As indicated in the responses that follow, we have taken all these comments and suggestions into account in the revised version of our paper.

Comment #1
It is a study on an important public health issue. The study makes an important contribution to the existing literature on economic burden of stomach cancer. In various places, authors indicating that they are estimating social burden of stomach cancer. The Cost-of-Illness (COI) methodology cannot estimate social burden. COI is used to estimate only economic burden (productivity losses plus cost of treating a disease) of disease. It is only the willingness-to-pay approach that can be used to estimate the societal burden of any public health problem.

Response
Base on the reviewer’s advice, we used “economic burden” rather than “social burden”. (p.4; l.14, l.15, p.13; l.13)

1. Abstract
Comment #2
Under Background, the statement of the purpose or objective of the study needs to be rewritten for clarity, e.g. “The objectives of this study were: to estimate and project the economic burden associated with stomach cancer in Japan; and to identify the key factors that drive the economic burden of stomach cancer.”

Response
We revised it as follows; “The objectives of this study were to estimate and project the economic burden associated with stomach cancer in Japan, and to identify the key factors that drive the economic burden of stomach cancer.” (p.3)

Thank you for your precious advice.

Comment #3
Under Methods, there should be mention of the direct and indirect costs of the COI methodology.
Response
We added description as follows; “We calculated direct cost and indirect cost (morbidity cost and mortality cost), and estimated the COI by summing them up.” (p.3)

Comment #4
Under Results, the authors should provide the total direct cost, total indirect cost, the grand total cost, and grand total cost per case of stomach cancer.

Response
We added them in Abstract as follows; “Morbidity cost was 85.6 billion yen and 54.0 billion yen, mortality cost was 972.3 billion yen and 806.4 billion yen, and mortality cost per person was 19.4 million yen and 16.1 million yen in 1996 and 2008, respectively.” and “Mortality cost per person is also predicted to decrease (9.5-12.5 million yen depending on the model in 2020).” (p.3)

2. Background
Comment #5
a) Authors should provide one or two paragraphs reviewing findings of published stomach cancer studies conducted in Japan and other countries.

Response
We revised as follows; “Most of them, moreover, are limited to the estimation of direct medical expenses, only in one time-point or cost-effectiveness of Helicobacter pylori eradication [2-4]. Koinuma estimated that cost (direct cost, morbidity cost and mortality cost) of stomach cancer was approximately 1,400 billion yen in 2005 [3]. The incidences of stomach cancer differ greatly by country. It is known to be high in Japan and to be low in the United States and Europe. Low incidence and limited social burden might explain for the scarcity of studies about cost of stomach cancer in those countries. Furthermore there are few long-term estimations or future predictions of economic burden of stomach cancer.” (p.4)

We also mentioned in Discussion about the studies of other countries and Helicobacter pylori eradication as follows; “There are several studies reporting economic effects of Helicobacter pylori eradication [4, 25], and Helicobacter pylori eradication might reduce healthcare cost of stomach cancer. Our study does not take the effect of a
specific treatment technology into consideration, and further study of COI including the possible effect of *Helicobacter pylori* eradication treatment would be needed.”

Comment #6
b) In the last paragraph, the authors should restate the objectives of the study as suggested in the Abstract above.

Response
We revised as follows; “The objectives of this study were to estimate and project the economic burden associated with stomach cancer in Japan, and to identify the key factors that drive the economic burden of stomach cancer.” (p.4)

3. Methods
Comment #7
a) The formulas used in estimating COI should be presented as equations to enable the readers to see how the calculations of costs of premature deaths, costs of morbidity (non-fatal disability) and direct costs of diagnosing and managing/treating stomach cancer. Although the authors are dealing with a different disease, we would encourage them to browse through a study using similar methodology reported available at the following link:
http://www.biomedcentral.com/1472-698X/9/6

Response
We inserted the equations in Methods. And we added the list of abbreviations at the end of Main Text.

Comment #8
b) The authors should include a table containing the assumptions made in the course of estimating the costs mentioned above. They should also provide rationale for making those assumptions. For example, if the assumed discount rate is 3%, it would be important to justify the choice of that rate.

Response
→ We added the reason that we used 3% as discount rate. It is the following sentence, “because 3% is widely used as discount rate in the United States, where the application of the COI method was popular.”(p.6)
And we made a new Table as Table1, and showed the elements used for calculation. We added the description as follows; “The elements used for calculation in future prediction of COI are shown in Table 1.” (p.7)

Comment #9

c) In the first paragraph, 2nd sentence, the authors state that “The COI method has been used widely to evaluate the burden of illness since 1960s, and has been used for policymaking”. COI studies cannot be used for policy making or decision-making. They can only be used for advocacy purposes to raise awareness of a specific public health problem. The authors should read the following: Shiell A, Gerard K, Donaldson C. Cost-of-illness studies: an aid to decision-making? Health Policy 1987;8:317–23.

Response

We understand that there is the criticism against the COI method. Therefore, we introduced the pros and cons about COI citing several examples and made our position clear. The following sentences were inserted in Discussion. “The COI method was used in our study since it has been used widely to evaluate the burden of disease since 1960s, and has been used for policymaking [15-19]. There are reports that the COI method has been used in several countries and international organization [20, 21]. On the other hand, there is also the criticism against the COI method that COI studies can be used for advocacy purposes and it cannot be used for policy making or decision-making [22]. We consider that the COI method is suitable for time series comparison and future prediction of the economic burden because of its simplicity, admitting the availability and effectiveness in policy-making are still to be demonstrated.” (p.12)

4. Results

Comment #10

In addition to what the authors have already reported, they should conduct and report on sensitivity analysis, i.e. they should vary the key assumptions to see the impact on their findings. This is important to see how robust their estimates are. For example, what happens when you use a discount rate of 10% instead of 3%, etc.?

Response

We added the description about the sensitivity analysis in Discussion as follows; “In our analysis, the main model is the mixed model. The fixed model is a reference. The
logarithm model is the low-end, and the linear model is the high-end estimation, respectively, and they can be regarded as sensitivity analyses showing the robustness of the mixed model.” (p.10)

Although we conducted the sensitivity analysis which changed the discount rate (0%, 5%) in order to evaluate the robustness of our estimation result, the tendency of result was consistent in comparison with the estimation in case of 3%. When discount rate was 0%, COI was estimated at 1,567.4 billion yen in 1996, 1,484.8 billion yen in 2002 and 1,323.1 billion yen in 2008. When discount rate was 5%, COI was estimated at 1,170.1 billion yen, 1,120.7 billion yen and 1,018.1 billion yen, respectively. As for discount rate, we cannot adopt the discount rate that is far from real interest. Nowadays developed country’s interest rate is quite low. So we adopted 3% as discount rate.

5. Discussion

Comment #11

- Authors should indicate how their estimates for Japan compare with the costs of stomach cancer obtained in other countries. A Google search will enable them to identify relevant studies conducted and published on other countries.

Response

We added the description as follows: “There are several studies reporting economic effects of *Helicobacter pylori* eradication [4, 25], and *Helicobacter pylori* eradication might reduce healthcare cost of stomach cancer. Our study does not take the effect of a specific treatment technology into consideration, and further study of COI including the possible effect of *Helicobacter pylori* eradication treatment would be needed.” (p.13)

We cannot find the articles that estimated COI of stomach cancer in other countries. The reason why is not clear, but the incidence of stomach cancer is low and social burden of stomach cancer is limited in the United States and Europe, and the fact may explain for the scarcity of reports. Most of studies concerning cost estimated the economic effect of *Helicobacter pylori* eradication. Our study does not take the effect of a specific treatment technology into consideration, and it is difficult to compare the reported effect of eradication with the result of our study.

In a Google search, we were able to obtain the information about the cost of the stomach cancer like National Cancer Institute in United States, etc. However, since the
methodology of calculation is not clear, we considered it was difficult to cite them as references.

6. Conclusion
No comments.

7. References
Comment #12
The authors should look again at their references to ensure that they adhere to referencing style of the journal.

Response
We are very sorry, we revised them correctly.

Finally, we thank Dr. Kirigia (reviewer 2) constructive comments that have helped to improve our manuscript. Looking forward to hearing from you.

Yours truly,

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