Author’s response to reviews

Title: Estimating lifetime economic burden of stroke according to the age of onset in South Korea: a cost of illness study

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Author’s response to reviews: see over
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Journal Editorial Board
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RE: REVISED MANUSCRIPT OF RESEARCH ARTICLE (MS: 7312901153814292)

ESTIMATING LIFETIME ECONOMIC BURDEN OF STROKE ACCORDING TO THE AGE OF ONSET
IN SOUTH KOREA: A COST OF ILLNESS STUDY

Dear Journal Editorial Board,

Thank you for considering our revised manuscript for publication in the BMC Public Health.

We are grateful for the Referees’ comments which were very helpful in improving the quality of our work.

Please find the attached revised manuscript with changes highlighted, which addressed points that Referees commented.

We have provided our specific answers giving a point-by-point response to each of the Referee’s concerns in the following pages.

We thank you for your time in reviewing this revised manuscript and look forward to the good news.

Yours sincerely,

Hae Sun Suh, on behalf of the co-authors
Major compulsory revisions

A. Measurement of costs.
   - Are all relevant costs included from the societal perspective which include more than the health sector and patient. Nursing home costs may be separate from acute hospitals. Carer costs outside hospital sector? Uninsured medical costs need to be defined to satisfy this query. Costs to business and government do include the consideration of appropriate productivity costs and welfare impacts (disability pensions) if there are any. Who cares for stroke victims that are unable to work, that do not stay in hospital?

   - [Authors’ response] This comment is reflected in revised manuscript line 187-193, 199-202, 242-248, 255-259 and 261-267. We added categories of cost components used in this study to help readers clearly understand our study results. Costs were categorized as costs inside health sector, costs outside health sector, and costs resulting from loss of productivity. In each category, we addressed the queries from referees in detail in lines mentioned above. For welfare impacts, we did not include these in our analyses because these were regarded as transfer costs. In addition, we almost don’t have disability pensions or sick leaves for stroke in Korea unless the reason of stroke is job-related, which is difficult to prove.

B. Measurement of health states and loss of productivity.
   - Measurement of years of productive life lost needs expansion:
   - Fatal stroke = loss of productive years to 65 from age at stroke
   - Non-fatal stroke = if serious and must retire early due to ongoing disability: loss of productive years from age of stroke: ie a serious stroke is the same as a fatal stroke. If not serious: the loss of productive years= absence from work due to medical visits, recuperation time post hospital and hospital time following stroke.

   - Ignoring the distribution of severity of stroke may cause distortions across the age groups and genders leading to either under or overestimation of the impact of stroke on years of life lost. Your simplified treatment requires justification.

   - [Authors’ response] This comment is reflected in revised manuscript line 124-126, 152-158, 450-454, and 460-463. We have added our justification for not fully considering the distribution of severity of stroke and mentioned this point as one of our study limitations, where further research is needed.

C. Valuation issues.
   - Friction Cost and Human Capital generate very different results and both should always be presented as a sensitivity analysis. Which one is more appropriate depends on the research question and needs to be discussed as they measure different aspects of the same issue. Is this a societal perspective? If the unemployment rate is high then fatal stroke victims can be replaced within 3 months. If unemployment is low then it may take longer for a person to be replaced possibly 6 months. New persons enter the workforce through ageing
and immigration all the time.

- **[Authors’ response]** This comment is reflected in revised manuscript line 383-412. To meet our study objective, the human capital approach is appropriate than the friction cost approach. We have listed the reasons in revised manuscript line 392-400. We also performed sensitivity analyses by using the friction cost approach with a 6-month friction period (due to the lower unemployment rate compared with the average unemployment rate in OECD countries) and employer costs of US dollar 362 per employee on training in 2000 (Marquardt MJ, et al. 2002). We extrapolated training costs in 2000 to 2008 value using the overall annual consumer price index (129.3 in 2008 based on 2000). As expected, we got lower estimates for loss of productivity from this sensitivity analysis than the estimates from using the human capital approach. Although above reference was the best available evidence to employ the friction cost approach, there were too many uncertainties existing in the data we used. We searched published literatures or reports intensively to find the Korean data needed for the friction cost approach, but failed to identify the needed estimates. We also contacted government organizations in Korea (Departments related to Human Resources and vocational training in Ministry of Strategy and Finance and Ministry of Employment and Labor) to seek expert opinions of these estimates, but it was not successful.

- Minor essential revisions
  A. Why are there productivity costs due to morbidity past 65 when there are no productivity costs due to fatal strokes past 65 in Appendix tables 1 and 2.

  - **[Authors’ response]** This comment is reflected in revised manuscript line 273-275 and in Appendix Table 1 and Appendix Table 2. We redid the analysis by not including productivity costs due to morbidity past 65 in both patients with non-fatal stroke and those with fatal stroke. All the related numbers are changed accordingly in the manuscript and tables.

  B. “In calculating future costs, we did not allow for increases in healthcare costs (including from inflation) nor did we discount future costs to the present value, as these opposing effects were similar in magnitude and hence would have nullified one another” This statement needs further justification and discussion. Were the rates of inflation in Korea only 3%, as is the discount rate preferred by Gold et al. If the inflation rate was higher, the conclusion is invalid. Needs a reference to support the claim.

  - **[Authors’ response]** This comment is reflected in revised manuscript line 193-197 by providing the reference to support this claim.

  C. Equity issue that should be addressed =that women and men have a differential economic impact of stroke, due to different general population life expectancies and differential work force participation rates and rates of pay within the work force. Currently the argument would support prevention of stroke in men primarily. Is this in accord with social values in Korea?

  - **[Authors’ response]** This comment is reflected in revised manuscript line 380-382 and 455-459.
D. ‘Looming economic calamity’ needs to be expressed more scientifically since the number of strokes in the young is still small, may be rising, but from a very low base and only across a small time period, and has been valued with an exaggerated valuation system not tested in sensitivity analysis with an alternative (Friction Cost)

- [Authors’ response] This comment is reflected in revised manuscript line 56 by deleting this expression.

- Discretionary revisions
  A. There are a number of isolated typographical errors that also need correction.
  - [Authors’ response] This comment is reflected in revised manuscript.

B. Column headings in Appendix Tables need definition and explanation for the international audience.
  - [Authors’ response] This comment is reflected in revised Appendix Table 1 and Appendix Table 2.

C. Productivity losses need to be labelled and used consistently (lost to productivity?)
  - [Authors’ response] This comment is reflected in revised manuscript as “loss of productivity” consistently.
<Referee 2>

This is a well designed analysis of the lifetime cost of stroke in Korea using insurance claims data. Although the data may or may not well represent the true data on cost of stroke treatment, they can be used as a good proxy proving the limited time and resource needed for new data collection. It would be more interesting, however, to see whether the true cost of treatment differ from the claims. The authors may consider collecting the former data at some treatment centers using the unit cost approach (i.e. cost of drugs, cost of health personnel time, cost of laboratory tests, etc.)

[Authors’ response] This comment is reflected in revised manuscript line 460-463.

The manuscript is well written. Some typing errors were noticed (see below), and some phrases and sentences need some more clarification. I suggest some discretionary revisions as shown below:

1. Abstract: Line 36-37
   A. It will be clearer to understand if more information on the method in the abstract is added. For example, sources of transition probabilities for other states (e.g. incidence), and costs other than the medical cost.
   [Authors’ response] This comment is reflected in revised manuscript line 35-48 by adding more information about methods we used in this study.

2. Background: Line 62
   B. Need a space between ‘assign’ and ‘greater’.
   [Authors’ response] This comment is reflected in revised manuscript line 72.

3. Methods
   A. Line 89-90: Could the authors show the number of stroke cases for each cohort in Table 1?
   [Authors’ response] This comment is reflected in revised Table 1 by adding the number of stroke cases for each cohort.

   C. Line 161: It is not clear to me why risks (Rfs, Rnfs, and Ds) were converted to probabilities using the formula p=1-e^-rt. As observed, when t (length of cycle) is 1, p is equal the risk.
   [Authors’ response] When t is equal to 1, p is not equal to the “risk” in this formula as Referee2 commented. Thus, we added the reason of using this formula in the revised manuscript line 178-182.

   B. Line 192: Please explain more what the cost of a fatal stroke is and add a reference. Do I understand correctly that this is also the cost of treatment? How is it different from the cost of treatment in the first or second year? Why is it more expensive?
   [Authors’ response] This comment is reflected in revised manuscript line 214-217, 224-229 and 232-235. The cost of a fatal stroke is costs occurred in patients who died within one year after the stroke onset. The first or second
year cost only applies to a non-fatal stroke case. The costs of fatal-stroke are more expensive than costs for non-fatal stroke because the fatal-stroke case is more severe than the non-fatal stroke.

D. Line 202: If possible, please explain why the transportation cost for outpatient is much cheaper than the transportation cost for admission.

   - [Authors’ response] This comment is reflected in revised manuscript line 251-254. Transportation costs for outpatient are cheaper than those for admission because patients usually visit clinics located nearby for outpatient visits in general.

E. Line 203-204: May consider deleting (1,000 KW is approximately equal to 1 US dollar) because it appears twice in the same page.

   - [Authors’ response] This comment is reflected in revised manuscript line 245-246 by mentioning this once.

F. Line 221: Please give an example of how to calculate the out-of-pocket spending for the second year (and beyond) using the ratios of insurance-covered second-year to the first year costs. Specifically, it is not clear how the two underlined phrases relate? Perhaps, move the method used for sensitivity analysis into this section.

   - [Authors’ response] This comment is reflected in revised manuscript line 267-270. We added an example as Referee 2 commented in footnote d of Appendix Table 1 as “For the second year, it was estimated using the gender- and age-specific ratios of second-year to the first-year medical costs. For example, the cost of 291,677 for 45-year old male was calculated as: 1,653,801 \times \frac{535,078}{3,033,876}”.

4. Results

   A. In Table 3, please make sure that the cost of fatal stroke for men and women aged 85 at stroke onset does not include the cost of premature death.

      - [Authors’ response] This comment is reflected in revised Table 3 by making sure that the cost of premature death was not included in the cost of fatal stroke for men and women with stroke onset age at 85 years.

   B. In addition, could the authors show the cost of illness with the distinction between the cost of treatment, out of pocket cost, and productivity cost?

      - [Authors’ response] This comment is reflected in revised manuscript line 307-310 and revised Appendix Table 1 and Appendix Table 2.