Author's response to reviews

Title: Acute and Chronic Impact of Cardiovascular Events on Health State Utilities

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Author's response to reviews: see over
Responses to Reviewers’ Comments on the Manuscript titled “Acute and Chronic Impact of Cardiovascular Events on Health State Utilities”

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In this document, we have listed all comments from the two reviewers. After each comment, our response is presented in bullet points. All edits and additions within the manuscript itself are highlighted in yellow.

COMMENTS FROM REVIEWER 1 (Wen Ye)

We thank this reviewer for the thoughtful comments and categorizing our paper as “an article of importance in its field.”

1. This paper used an interesting approach. But it does have all the caveats the authors have discussed in the conclusion section. Utility scores are heavily influenced by the description given by the interviewed doctors. Because they used the same description for each health states, the utility scores does not catch the potential wide range of conditions, therefore the utility scores should have more variability than shown in the paper.

   • From this comment, it appears that the reviewer agrees with the limitations that we have listed in the discussion section. It does not seem that the reviewer is recommending any changes to the paper in this comment.

2. Statistically, it would be more appropriately to conduct a global test before doing all the pair-wise comparison to control for inflated type I errors due to multiple comparisons. But since the p-values are small, it wouldn’t make any difference to the conclusions.

   • As this reviewer says, the p values are quite small, and the global test would not alter the conclusion. Furthermore, the primary purpose of the current paper was to provide the mean utility estimates, rather than statistical testing of a specific hypothesis. Therefore, we would prefer not to add additional statistical testing to the manuscript, and it seems like this reviewer is generally satisfied with the current approach. However, if the editor would like to see another statistical test, please let us know.

3. I would also suggest the authors use graphically method to present their results.

   • We thank this reviewer for the good suggestion. In response to this comment, we have replaced the table with utility descriptive statistics (originally called Table 2) with a bar graph (Figure 2).
COMMENTS FROM REVIEWER 2 (Rui Li)

We thank this reviewer for the helpful comments below and these kind words about our study: “The study design is well developed and thoroughly described. The discussion supports the data and compares the results from other studies reported in the literature, and the study limitation is thoroughly described.

1. In the paragraph under “participants”, the authors stated that “inclusion criteria did not specify particular clinical characteristics because interviews were intended to yield utilities that may be used in cost-utility analyses for submission to health technology assessment agencies, most of whom prefer that utilities represent general population values.” How are the characteristics of the UK general population compared with the study participants reported under “Sample description”? Although the authors discussed it as a limitation, it will be informative to report how different the study participant from the general population in UK, especially the rate of having these cardiovascular events, so the readers will have a sense how generalizable the study results are.

- The discussion section includes the following paragraph, which addresses this issue: “The sample recruitment strategy should also be acknowledged as a limitation of the current data. Utilities were based on evaluations of a general population sample because most health technology assessment agencies prefer that utilities represent the general public or societal view [59-62]. However, the sample was recruited in only two UK locations, and it should not be considered nationally representative. The extent to which the current utility scores would differ from values derived in a nationally representative sample is not known.”

- Although this study was conducted with a sample of participants recruited from the general population, it was not recruited to be nationally representative, and the manuscript does not state that the sample is nationally representative. Still, as this reviewer suggests, it is possible to compare demographic characteristics of the current sample with characteristics of the UK population:
  - Gender: Recent UK census data includes somewhat more women than men (Male 49%; Female 51%). This pattern was similar in the current study sample (male 45%; female 55%).
  - Age: The current sample had a mean age of 46.6 years and a median age of 49.0, which is somewhat older than a 2014 estimate of the median age of the UK population (Male: 39.2 years; Female: 41.6 years; Total population: 40.4 years)
  - Ethnicity: The current sample had a lower percentage of white participants (78.0%) than the UK general population (87.2%)
Across these demographic categories, although differences between the current sample and UK population are apparent, the current sample is roughly similar to the overall UK population.

- We have not added this information to the manuscript because a comparison of the current sample’s demographic characteristics to those of the UK general population is likely outside the scope of this paper, and we are hesitant to make the paper longer. However, if the editor would like any of this information included in the manuscript, we can add it.

2. Did the author consider clustering effect of the two sites when comparing the difference between health state utilities? Because the study participants within the city are not independently and identically distributed, when conducting statistical analysis, clustering effect should be adjusted.

- Although there were some differences in mean utilities between the London and Edinburgh samples, the pattern of utility values was the same. Because the primary statistical outcomes of this paper are mean utility values, we are not sure exactly what type of clustering effect adjustment the reviewer is suggesting. Further, in general there does not appear to be evidence of a consistent (across studies) and systematic relationship between socio-demographic factors, such as region, and utility scores. If the editor thinks additional analyses should be conducted, please let us know what would be a useful addition to the manuscript, and we will run the analysis.

3. The last paragraph under “Utility interview procedures and scoring,” the first sentence, “If participants indicated that a health state was worse than dead, the interviewer altered the task so that respondents were offered a choice between immediate death (alternative 1) and a 1-year/10-year life span (alternative 2) beginning with varying amounts of time in the health state being rated, followed by full health for the remainder of the time horizon.” It was hard to understand “beginning with varying amounts of time in the health state being rated, followed by full health for the remainder of the time horizon.” Consider to rewrite.

- We thank this reviewer for highlighting this potentially confusing sentence. In response to this comment, we have added an example for clarification: “…beginning with varying amounts of time in the health state being rated, followed by full health for the remainder of the time horizon (one example of alternative 2 with a 10-year TTO task would be three years in health state D, followed by 7 years in full health).”

4. In Table 1, please explicitly state what “other” includes for marital status and employment status, because they are a large proportion of the study participants.

- As recommended by this reviewer, we have added this information to Table 1.
5. The second footnote under Table 2, should it be -0.85 instead of -0.95 for the lowest possible utility value for chronic health states reflected from the lower bounds of the chronic post-event health states under “Range” column?

- In response to a comment from the other reviewer, we have replaced this table with a figure. The figure reports means and standard deviation, but unlike the previous table, the figure does not include the range. Therefore, this footnote is no longer applicable.