Author's response to reviews

Title: Empirical analysis shows reduced cost data collection may be an efficient method in economic clinical trials

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Empirical analysis shows reduced cost data collection may be an efficient method in economic clinical trials

Comments of Reviewer Zia Sadique

- **Comment:**
The main objective of this paper has been to assess the validity of incomplete cost data collection concerning precision and accuracy of cost estimate, but the applied statistical methods only looked at mean or bias. The precision of cost estimate needs to be examined.

**Response:**
We thank the reviewer for his comment regarding the precision of cost estimating. On page 12, we now describe how precision was studied by comparing the standard deviation of the respective estimates. The new Table 6 illustrates the precision regarding change in standard deviation due to incomplete data collection (page 14). We hope that with this additional information it will now become clearer by providing overview information about the percentage change.

- **Comment:**
The results show that some cost categories are less biased when incomplete data collection is used, but the result of this study is relevant to the specific context of patients with acute myocardial infarction. It should be recognised that generalisability of this study results is limited unless validated externally or compared in some other context.

**Response:**
We are aware that generalisability of the results is limited to studies with similar treatment patterns over time. By rearranging and adding the respective sentences on page 17 and pages 18,19, we have made this clear.

- **Comment:**
The mean estimate can be sensitive to sample size, which needs to addressed and recognised.

**Response:**
We are not sure whether we really understand the comment. We analysed the change in required sample size assuming ceteris paribus where α, β and the expected mean difference in costs are not changed. In this case, an increase in sample size has no influence on the mean estimate but on the mean estimate precision. Because of this, a larger sample size is required to keep the power. To clarify this, two sentences on page 12 have been modified.
Comment:
The costs are reported in 2008 prices. In the KORINNA trial patients were enrolled between 2008 and 2010, and so the costs would be better represented in more recent price level.

Response:
We agree that the costs or differences in costs between the control and intervention groups from the KORINNA trial should be reported at more recent price levels. However, as the differences in costs resulting from variable collecting scenarios were addressed in our study, the reported costs in 2008 prices are equally as applicable as costs at a recent price level.

Comment:
In the study design section, make it clear what was the comparator in cost effectiveness analysis of the KORINNA trial.

Response:
On page 7, we have added the sentence: The control group received usual care.

Comment:
The paper is about methods comparing complete versus a number of incomplete data collection scenarios. And this is tested using data from a randomised controlled trial. It would be clear for the reader to follow if this is mentioned in the background.

Response:
On pages 6 and 7 we have mentioned this in the background.

Comment:
Quality of written English: Needs some language corrections before being published

Response:
We have sought the assistance of an English language editor.
Comments of Reviewer Colin Ridyard

• **Comment:**
  1. Page 5, line 14: better to put: "cost data collection in clinical trials can be burdensome and can increase both the costs..."

  **Response:**
  We have changed the sentence on page 5 as proposed.

• **Comment:**
  2. Page 5, line 20: can additional references to trials involving patient recall in Germany and the US be included here as reference 8, although relevant, involves reference to UK clinical trials.

  **Response:**
  We have added two additional references.

• **Comment:**
  3. Page 6, line 2: it would be useful if the authors could quote one or two references supporting the statement "...unlikely that participants will complete all diaries"; alternatively state whether this is something they, too, have observed in the course of their own studies.

  **Response:**
  We have added one reference.

• **Comment:**
  4. Page 15, line 16-18: useful to mention here that patient report on hospital stays could be cross-validated against electronic hospital records where these exist.

  **Response:**
  We have mentioned this on page 16.

• **Comment:**
  5. The 'health warning' on lines 27 (p.16) and 1 to 6 (p.17) [Applying incomplete...TO ...or literature research] ought to be placed in the conclusion as well.

  **Response:**
  We have placed an abbreviated version of the 'health warning' in the conclusion as well (page 20).