Author's response to reviews

Title: Determining initial and follow-up costs of cardiovascular events in a US managed care population

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Author's response to reviews: see over
Reviewer Comments:

Reviewer #1:

- Overall I found this to be a generally well-written paper providing important information on CV costs in a US context.

- The background seem to be quite short - you state there is a lack of up to date cost estimates in the literature but perhaps a little more detail could be included here. In the first paragraph of the background you state that "most health economics cost analyses broadly consider CV disease rather than specific CV events". Again, a little more detail with perhaps reference to studies may be useful here.

In order to address these points, we have expanded the background by providing the average cost per discharge for Medicare patients with a principle diagnosis of CV disease from the 2010 update of the American Heart Association’s Heart Disease and Stroke Statistics.

- Within the first paragraph of the Data sub-section of the Methods section, there are lists of ICD-9 codes. I think these may be easier for readers to digest if they are in a table rather than in the main text.

As recommended, the lists of ICD-9 and CPT-4 codes have been deleted from the text within the Methods section and included as Table 1.

- In the sub-section Patient selection, (and this may be due to my lack of indepth knowledge of the US health care system as I am UK based) one of the excluded groups is patients “>= 65 whose insurance cover was not Medicare Risk”. Obviously in terms of age this is a key group, but in terms of their insurance coverage, is this a very small group of patients? If not, this could be quite an important group – and are they different in any way i.e. be a sub-group at even greater risk of CV events?

These patients are excluded because complete claims histories may not be available for patients without Medicare Risk coverage due to benefit coordination issues with other payers (we have added this explanation to the exclusion criteria section). In this database, about 10% of all people over 65 are enrolled in a Medicare Risk product (this is not necessarily consistent with the entire US over-65 population); although we can speculate about how these Medicare Risk patients differ from the non Medicare Risk population, we have no direct way of knowing if Medicare Risk patients are different from the rest of the elderly population. We were careful to specify "in a US managed care population” in the title of the article, to emphasize that we have included only patients covered by managed care plans.
Reviewer Comments:

Reviewer #2:

- In their paper, Chapman and colleagues aim to evaluate the initial and follow-up costs of CV events in a US managed care population.

- In the introduction, the justification for this study is the ‘lack of up to date cost estimates for specific CV events’. The stated objectives were
  1. Determine overall costs of initial and subsequent CV events
  2. Examine costs of 1, 2 and 3 year follow-up care in patients with CV event
  3. Compare total costs of follow-up care for patients with CV events compared to typical patient, with similar demographics.

- A major concern I have is that the stated justification and the subsequent objectives are not in line. If cost estimates for specific CV events are not available, should this not be the focus of the study, rather than objectives 2 & 3? There is not attempt to look at downstream costs, based on the initial CV event type, which would appear to be the more rational follow-up to objective 1. Please comment

  Continuing improvements in medical care make contemporary assessments of costs relevant and necessary for up-to-date economic analyses. The main objective of our study was to evaluate overall inpatient costs for index hospitalizations for CV-event subjects. Costs of index hospitalization for specific CV events were presented in order to illustrate how costs vary by CV event type. We considered that providing downstream costs for all CV event types would mean the inclusion of an overwhelming amount of data for a publication of this type and therefore restricted follow-up analyses to overall CV costs. However, in order to address this reviewer’s concerns, we have modified the background to clarify the rationale behind this study, specifically addressing the need for objectives 2 & 3.

- I do not understand why one would look at objective 3...this seems to be obvious that CV patients would have greater costs, especially as there was no requirement that the control patients have had a hospitalization...hence they are almost certainly a healthier group. As the authors themselves state, it is know that patients with CV disease have 3-4 times the downstream cost. What novel insight do the authors believe one gets from this analysis? Would it not be better to look at the drivers of cost within the CV group, in regards to the initial event, as stated as the primary justification for the study?

  We concur that it is fairly obvious that CV patients would incur greater costs than matched controls. However, as stated previously, we consider that continuing improvements in medical care and the pertinence of the setting examined (a nationally representative US managed care population) make such contemporary assessments of costs relevant and necessary for up-to-date economic analyses. In particular, we believe that the incremental costs incurred by CV patients would be useful information for multiple stakeholders in deciding how to most efficiently allocate healthcare resources.
Methods

- Patient selection: Exclusions included “patients > 65 years whose insurance was not “Medicare Risk” at any time during study period”. Please elaborate why this is a necessary exclusion

  As stated in a previous response, these patients were excluded because complete claims histories may not be available for patients without Medicare Risk coverage due to benefit coordination issues with other payers. We have added this explanation to the exclusion criteria section.

- Authors comment on covariates that they are adjusting for, prior to a comment on the model they are using and why. I would suggest they reorder this.

  The paragraphs have been reordered to address this point.

- “A generalized linear model was used to account for remaining differences in variables used to match patients” : Was a matched regression analysis done? Appears to me that all subjects (CV and control) were entered into a typical GLM model...ie was special methods used for matched-data.

  The reviewer is correct that a matched regression modelling technique should be used for this analysis. We have run the regression analysis using generalized estimating equation (GEE) modelling rather than the prior GLM regression, and have updated the relevant table and text to reflect this new analysis.

- For the GLM model, what distributional family was used and what link function? The authors need to specify this and why a particular choice was made. Moreover, guidance as to the interpretation of the B-coefficients in Table 4 requires this. It seems that a log link was used, in which case the exponential of the coefficients should be presented and explicitly stated that these are ratio of the means.

  Because we were modelling a positive, continuous and skewed response variable (costs), the GEE model uses a gamma distribution with log link function. We have added this information to the text. We have also presented the results in Table 4 as the exponential of the Beta-coefficients, with 95% confidence intervals, and have explained how to interpret these in the Results section.

- How did the authors deal with the fact that they use a naïve estimator of mean cost, by only including noncensored cases. From figure 1, it appears that only 40% of the total patient sample was continuously enrolled for 1 year. The 80% of patients excluded were presumably loss to follow-up (b/c patients who died were included as complete cases). The authors must comment on the bias that this will introduce into their estimates. Almost certainly this will bias mean costs towards patients with shorter follow-up (ie who died soon after hospitalization), and therefore I believe towards sicker patients, with inflated costs.

  We have acknowledged and discussed any potential bias within the study limitations paragraph of the discussion.

Results
Some comment on the fact that of the almost 200,000 patient initial identified, only 29,863 were studied.

*Text has been included at the beginning of the results section explaining that the majority of patients were excluded, predominantly for not fulfilling continuous enrolment requirements or for having a CV-related claim in the pre-index period*

In paragraph 2, initial CV-specific costs are given. I believe it would be of interest to know follow-up costs, stratified by these initial event types.

*As stated in a previous response, we considered that providing downstream costs for all CV event types would mean the inclusion of an overwhelming amount of data for a publication of this type and therefore while costs of index hospitalization for specific CV events were presented, follow-up analyses were restricted to overall CV costs.*

The differences between CV and controlled patients is obvious...again, I am not sure of any new insight from this.

*As stated in a previous response, we consider that continuing improvements in medical care and the pertinence of the setting examined make such contemporary assessments of costs relevant and necessary for up-to-date economic analyses. In particular, we believe that the incremental costs incurred by CV patients would be useful information for multiple stakeholders in deciding how to most efficiently allocate healthcare resources.*

The multivariable model should be better explained, especially the interpretation of the beta-coefficients (are these log of the ratio of means etc)

*As stated above, we have now added this information to the text, and have explained how to interpret the multivariable model in the Results section.*

The results of the multivariable model are not that insightful, as no attempt is made to control for co-morbidities outside of DM, HTN and Hyperlipidemia. A more interesting model would be to look at just CV patients, and after controlling for co-morbidities, understand the impact of the initial CV event on downstream costs.

*Within the limitations section of the Discussion we have highlighted that the multivariable model used was adjusted for the presence of DYS, HTN and DM, and that is possible that inclusion of other co-morbidities may have affected the results of these analysis.*