Author's response to reviews

Title: Exploring the treatment delay in the care of patients with ST-elevation myocardial infarction undergoing acute percutaneous coronary intervention: a cross-sectional study

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Author's response to reviews: see over
Amsterdam, February 19th, 2015

Dear Dr. Morrey, Dr. Hochadel and Dr. Geraedts,

Thank you for your interest in our paper and your careful attention in revising it. This helped us a lot to improve it. On behalf of all authors I would like to present to you the revised version of the paper ‘Exploring the treatment delay in the care of patients with ST-elevation myocardial infarction undergoing acute percutaneous coronary intervention’ (MS: 2861301961364237). In the revised version, we have incorporated the recommended suggestions of the reviewers.

Below you will find a detailed description of our response to the reviewers’ suggestions, the changes made in the manuscript and the location of the changes. We hope this satisfies the wishes of the reviewers. If more information about e.g. the sensitivity analyses is required, please do not hesitate to contact me.

All authors have seen and approved the revisions and the revised version of the manuscript. We hope that the changes are satisfactory and the paper is acceptable for publication in BMC Health Services Research. We look forward to your decision.

On behalf of the authors.
Sincerely yours,

Joppe Tra
Exploring the treatment delay in the care of patients with ST-elevation myocardial infarction undergoing acute percutaneous coronary intervention: a cross-sectional study

Reviewer 1 - Matthias Hochadel

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<th>Comment</th>
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<th>Changes</th>
<th>Line #</th>
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<tr>
<td><strong>Major compulsory revision</strong></td>
<td></td>
<td>Changed previous Tables 179-180, 186, 218, 480 and further; introduced new Table 2; changed names of Tables</td>
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<td>It would be of interest to see a unmodified summary of the observed data. The authors should present a descriptive table (e.g. median and quartiles, number of observations) of the available data on treatment delay (as defined in the study), and the ischemic time (from symptom onset to sheath insertion) in total and in the subgroups transferred from other hospitals, with ECG made in the ambulance, by the hospital, and by the general practitioner.</td>
<td>Adding the unmodified summary of the observed data in addition to the imputed data provides an indication of the effect of the imputation procedure. As recommended by the reviewer, we have added the observed data, number of missings and % of missings per variable to the Tables 2 (patient characteristics) and 3 (admission characteristics) accordingly. In addition, to provide more insight in the time variables, we have added the requested table with the time variables per subcategory as Table 4. However, it should be noted that the differences in time are not corrected for the effects of other independent variables</td>
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<td><strong>Minor essential revisions</strong></td>
<td></td>
<td>Added information about the selection procedure of patient charts</td>
<td>83-85</td>
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<td>According to table 1, not all patients from the year 2012 were screened for the analysis in each hospital. When was the limit of the screening capacity reached? How were the screened cases selected?</td>
<td>Every month, the chart abstractors selected patients who were discharged in the previous month by means of the hospital financial system codes. As this selection procedure is highly sensitive but not very specific, all preselected charts were checked manually for the discharge diagnosis. Consequently, for each hospital, two chart abstractors attempted to screen as many patient charts as possible during 8 hour shifts for each hospital. However, given the extensive data required per patient combined with the availability of six chart abstractors, it was not possible to screen all patient charts. Therefore patients were included in chronological order of discharge date or date of death. This information was initially not mentioned in the paper as it was previously described in the study design paper as referred to in line 62, however, readers who are not familiar with this paper may miss this essential information. Therefore this was added to the manuscript.</td>
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In a subsample patient charts were abstracted by a second independent reader. Which decision was made in case of disagreement?

In case there were differences between the two readers, the original patient chart was consulted for the final decision. In the rare case that this did not result in consensus between the two readers, a local cardiologist was consulted for the final decision. Added information about the procedure in case of differences between chart reviewers 98-99

Do you have information on hospital mortality in this patient population?

After undergoing their PCI procedure, many patients were transferred from the PCI center to a non-PCI capable hospital for follow-up care, as is customary in the Netherlands. Because we were not allowed by Dutch privacy regulations to link the information of individual patients between hospitals, we were unable to obtain reliable information about the hospital mortality for these patients. Also, the in-hospital mortality of this population would have added little value as only patients who made it to the hospital were included in this study. Therefore the group of patients who were in the most critical condition could not included in this study, resulting in an unrealistically low estimate of mortality. Therefore adding information about in-hospital mortality would add little value to the results of this study. Added the lack of hospital mortality data to the limitations section of the paper 295-299

Does interhospital transferral mean that the ECG was done at a different hospital? Is it possible to differentiate between ECG done at the same hospital as the PCI, or other hospital?

Interhospital transfer in our study was defined as all patients who are transferred from another hospital to a PCI center. This includes patients who first presented to the emergency department of a hospital without PCI facilities. After initial diagnostic tests including an ECG, these patients are rapidly transported to a PCI capable hospital. Alternatively, an ECG was performed in the ambulance but there was no ST-segment elevation yet or it was not recognized as such. It is theoretically possible to distinguish between the location of the ECG, but due to the small number of patients this will not add much value to the current analyses. Added definition for interhospital transfer 39-41
Can you distinguish between electrocardiograms performed during vs. Outside normal working hours (Monday - Friday 8:00 - 18:00)? Are there differences in treatment delays?

Differences in treatment delay between office hours and after hours have been identified in previous studies, e.g. in the study of Magid DJ, Wang Y, Herrin J, McNamara RL, Bradley EH, Curtis JP, et al. Relationship between time of day, day of week, timeliness of reperfusion, and inhospital mortality for patients with acute ST-segment elevation myocardial infarction. JAMA. 2005; 294:803-12. In our study, we looked at the moment patients were admitted at the hospital instead of when the ECG was performed and categorized these as office hour presentation, weekend presentation or weekday evening presentation (Table 3). No significant differences between these patient groups were identified (p=0.92 for weekend and p=0.15 for weekday evening; see Table 3).

The delays caused by transfer from other hospitals or visit to the general practitioner might be felt to have additive effects on the time to PCI rather than multiplicative effects. Moreover, the authors report effects on the treatment delay in minutes. As a sensitivity analysis, could the authors 1) look at empirical density curves in the above-mentioned subgroups, and 2) repeat the gamma regression using an identity link instead of a log link?

Thank you for this excellent suggestion. We agree with the reviewer that according to the current model (GLM with Gamma distributed outcome and log link), effects are multiplicative instead of additive, which would be the case with an identity link. As the reviewer suggested, the histograms of the subgroups were re-evaluated. What we found is that only 5 patients in the non-imputed dataset had both an ECG at the GP and an interhospital transfer. Our study does not have the power to calculate reliable point estimates for these specific combinations of subgroups. As a sensitivity analysis, we re-ran the model for the observed data with an identity link instead of a log link and compared the results. What we found is that the larger delays (ECG at the GP, interhospital transfer) were even larger in the model with the identity link compared to the model with the log link, as would be expected. However, the size of the differences in the point estimates was relatively small (approximately 5 minutes) and the 95% confidence intervals overlapped. Although we are fully aware that the point estimates in minutes can differ between different statistical models, it does provide an easily interpretable measure for the 'size' of the delay. This helps clinicians to interpret our results. To point out this limitation, we added a warning to Table 5

Table 5

Added a warning to Table 5 about the interpretation of the delays in minutes.
Fixed effects for the participating centers were included in the regression model. Are the delays significantly different between the centers?

A variable for the PCI center was added to each statistical model for correction. The models indicated statistical differences between the hospitals. However, the geographic regions the hospitals were serving also differed in population as well as geographic size. Therefore we were unable to compare the differences between the hospitals, as it would be impossible to differentiate between differences between the organization of care, differences in regional size and other potential reasons for these differences. Consequently, no findings on this variable were reported in this study. However, it is of importance to explain this decision. We therefore added information to the discussion.

Confidence intervals are not appropriate as a measure of dispersion, as they depend strongly on the sample size. It would be preferable to show means with standard deviations instead of confidence intervals in the descriptive tables.

We agree with the reviewer that confidence intervals are strongly influenced by the sample size. From the average, the difference between the mean and the upper and lower confidence intervals and the sample size, the standard deviation can be calculated. For convenience purposes of the reader, we have followed the suggestion of the reviewer and provided the standard deviation instead of the confidence intervals.

Reviewer 2 - Max Geraedts

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<th>Comment</th>
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<td>It would be nice to consider &quot;Menees DS, Peterson ED, Wang Y, Curtis JP, Messenger JC, Rumsfeld JS, u. a. Door-to-Balloon Time and Mortality among Patients Undergoing Primary PCI. New England Journal of Medicine. 2013;369(10):901–9&quot; in the introduction and discussion.</td>
<td>We agree with the reviewer that addition of discussing the paper adds value to this paper. We have therefore added it to the discussion section and discussed it in the context of future research.</td>
<td>254-259</td>
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