Author’s response to reviews

Title: Implementation and acceptability of a heart attack quality improvement intervention in India: a mixed methods analysis of the ACS QUIK trial

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Author’s response to reviews:

Only updated files (MS file, tables, figures and supplementary files) are included in the revised version per request from editorial office. Email address of ACS QUIK investigators added to the title page and acknowledgements section.

Responses to specific reviewer comments are outlined below:

Reviewer #1: Implementation and acceptability of a heart attack quality improvement intervention in India: a mixed methods analysis of the ACS QUIK trial
This is a very interesting manuscript describing the development of the ACS QUIK intervention and evaluates its implementation, acceptability, and sustainability. I believe the manuscript would add insight and informational details supporting implementation and evaluation of large multisite interventions. It is unfortunate that the results do not provide any new insights regarding barriers or facilitators to implementation science. Yet, with more details of the individual contextual environments and the intervention interaction, the paper would be greatly strengthened.

There are some specific issues with the manuscript that could be addressed to strengthen its impact and contribution.

1. Overall: As the Background in the Abstract clearly states, "We describe the development of the ACS QUIK intervention and evaluate its implementation, acceptability, and sustainability." Yet, I found there was a lack of clarity and specificity regarding the "intervention" vs the "toolkit", while reading the manuscript. Multiple titles were used, such as: study, toolkit, trial, clinical trial, intervention, and toolkit intervention. To obtain a better understanding, I needed to read the initial published manuscript. Therefore, I would highly recommend being very specific in addressing the whole intervention or the specific toolkit components.

Response: We have improved the consistency of the language to “toolkit intervention” to make the understanding of the intervention clearer. We include specific mention of the intervention components in the abstract and methods section. We have removed “clinical” from mention of the trial itself to improve clarity.

Changes to manuscript: Changes made as outlined above throughout the manuscript.

2. The term participant is used throughout the manuscript and it is not clear if you are referring to the hospitals, providers, or the patients. Please be specific as to who the participants are.

Response: Thank you for this helpful comment. We have now specifically used the term providers (physicians), and patients as appropriate instead of the term “participant”.

Changes to manuscript: Changes made as outlined above throughout the manuscript.

3. Please go into further detail regarding the people involved in the interviews and the surveys. It appears that 22 were involved in the surveys and 28 in the interviews. Yet, the total of both = 39. Also, please clarify why 63 is used as the denominator, even though 2 people were recruited at each site and if these were the people surveyed and interviewed.

Changes to manuscript: Changes made as outlined above throughout the manuscript.
Response: Thank you for the clarifying questions. We interviewed 28 physicians, and 22 physicians participated in the survey. Two physicians from the same hospital were interviewed; therefore, the total number of hospitals participating in either survey or interview was 39. The denominator used was the total number of hospitals that participated in the ACS QUIK trial (i.e. 63 hospitals). In the Methods section we have mentioned that at least two or more people were asked to be part of a local hospital’s quality improvement team for training purposes to implement the ACS QUIK toolkit intervention.

Changes to manuscript (Methods, physician interview section):

“From November 2015 to December 2016, one of three interviewers (KS, RD MDH) conducted 28 semi-structured in-depth interviews of physicians from 27 hospitals in English, either in-person or by telephone.”

4. It would be important to understand the impact of the hospital type and size for each of the findings.

Response: Thank you for this comment. We have previously reported the lack of an interaction by hospital size or type in the primary outcome paper for the ACS QUIK trial (Figure 3 in JAMA. 2018;319(6):567-578.). In this report, we identify differences in the direction of effect in optimal in-hospital and discharge medication use based on higher versus lower implementation scores (i.e. hospitals with higher implementation scores were more likely to provide optimal in-hospital and discharge medical care compared with hospitals with lower implementation scores; Supplemental Tables III and IV).

Changes to manuscript: None.


Response: Thank you for this comment and for sharing this helpful reference article. We have now included a definition for mixed methods approach in the manuscript.

Changes to manuscript (Background section):

“Mixed methods research employs rigorous quantitative and qualitative research involving multiple types of data (survey questionnaire, in-depth oral interviews, text-messages) to maximize the strengths and counterbalance the weaknesses of each data type and aids in real-life contextual understanding of a research problem from multi-level perspectives.”
6. Methods Section:

a. The Formative work to develop the toolkit.

i. The qualitative work is described in detail, but little is discussed about the systematic literature review. None of these results are discussed in the Results section but then you do address them in the Discussion of which we have no reference in the results section. The final Toolkit is described in the Methods - should this not be a component in the results section? Please see below in the Discussion section as this part of the manuscript may be omitted and summarized using the reference to your previously published papers.

Response: Thank you for this comment. We have previously reported the systematic reviews that informed the toolkit intervention development in the ACS QUIK methods paper (Am Heart J 2017; 185:154-60) but not the qualitative methods and results. The toolkit intervention has also been reported in our primary outcome paper (JAMA 2018; 319: 567-578). The purpose of the current manuscript is to report the implementation and acceptability of the toolkit intervention, and thus we have not reported the toolkit intervention components in the Results section.

We have added the references to the systematic reviews that supported the toolkit intervention development.

We address the comments in the Discussion section below.

Changes to manuscript: References added.

ii. The Toolkit has 4 components described on pages 6-7: 1) Audit and feedback; 2) Checklists; 3) Educational material; 4) Access to online training. You then describe telephone messaging groups, quarterly newsletters, and comparison ratings to other hospitals - why are they not #5, #6, and #7 components of the toolkit?

Response: Thank you for this comment. The four core components of the ACS QUIK toolkit intervention were based on the empirical evidence with the goal of improving processes of care and clinical outcomes. The comparison rating was included in the feedback reports. The messaging groups and quarterly newsletters were introduced to improve the communication between the research coordinating centre and participating hospitals. These components were not considered to be part of the toolkit intervention because they did not provide relevant clinical information to improve process of care or patient outcomes.

Changes to manuscript: None.
b. ACS QUIK toolkit training - It appears this training was much more involved than just the toolkit. It appears there was the creation within each hospital of a "Quality improvement team" and these teams were "clinically" trained to decrease inappropriate thrombolysis, increase use of specific meds, and selection of reperfusion strategies. Therefore, these trainings were much more than the toolkit. Suggestion would be to label the sub-section b. ACS QUIK Trainings.

Response: Thank you for this comment. Once we developed the ACS QUIK toolkit intervention with four components, training was conducted at each participating hospital to demonstrate the use and implementation of the toolkit intervention. We have re-labelled this section as “ACS QUIK training at site initiation visit”.

Changes to manuscript (Methods section): Label changed as outlined above.

c. What is the difference between a code team and a rapid response team? These were not fully defined on page 7 line 12.

Response: Thank you for this comment. Code blue teams respond to patients with cardiac arrest or respiratory failure, and rapid response teams respond to patients who are decompensating but have not developed cardiac arrest nor respiratory failure.

Changes to manuscript (Methods section):

“…code blue teams to respond to patients with cardiac arrest or respiratory failure and rapid response teams to treat patients who are acutely decompensated but have not developed cardiac arrest nor respiratory failure.”

d. Page 7 line 27 identifies "zonal project coordinators". Who are they and what role do they perform?

Response: Thank you for this comment. Three zonal project coordinators were appointed for coordination of this large cluster randomized trial in Kerala to help with trial coordination, conduct on-site interim monitoring visits, and to ensure data quality and completeness. Zonal project coordinators also provided refresher training to hospital staff in cases where there was change in hospital personnel and communicated weekly with the central research coordinating centre in New Delhi/Gurgaon, India.

Changes to manuscript (Methods section):
“Additional training to new staff or refresher training to existing staff was provided by one of three zonal project coordinators during the study period who provided local training, monitoring, and support for the trial.”

e. Online surveys were sent to "all" site investigators. Please be more specific as there were 63 participating hospitals identified. Page 5, line 56-58 describes that each hospital identified 2 members of the quality improvement team to participate. Therefore, please be specific in how many surveys were sent out and what exactly a "site investigator" is.

Response: Thank you for this comment. Online surveys were sent via email to all participating hospitals (i.e. 63 hospitals). Each hospital was led by a physician who was designated as the site investigator. On Page 5, we described that each hospital identified two members for the quality improvement team was for the purpose of providing the training at the site initiation visit.

Changes to manuscript (Methods section):

“Audit and feedback reports were sent via email to the physician site investigator from each participating hospital every month but were reviewed by a minority of physicians.”

f. A discussion of the temporal trends and how they affected the intervention implementation would be useful.

Response: Thank you for this comment. Temporal trends in background clinical care and outcomes that were incorporated into the reporting of the primary and secondary outcomes in the ACS QUIK primary outcome paper (JAMA, 2018; 319: 567-578). However, we did not capture temporal trends in implementation or acceptability of the toolkit intervention. We are uncertain if or how this influenced the implementation of the toolkit intervention.

Changes to manuscript: None

7. Analysis Section:

Response: Thank you for this comment. We have used the COREQ checklist and attach it with our submission. We welcome specific comments or concerns about the analysis, which was overseen by experienced qualitative researchers (DV, SG).

Changes to manuscript: COREQ checklist added to submission.

b. The integration of the qualitative data into the mixed effects logistic regression was very interesting.

Response: Thank you for this comment.

Changes to manuscript: None.

8. Results Section:

a. Online survey - what was your response rate?

Response: Thank you for this comment. 22 providers/physicians from different hospitals responded in online survey out of the 63 hospitals. The response rate was 22/63 = 35%. We have clarified this in the Results section.

Changes to manuscript (Results section):

“Of the 63 participating hospitals, 22 physician site investigators (35% response rate) completed the online survey.”

i. How many and description of the intended recipients of the surveys would be good to know?

Response: Thank you for this comment. As mentioned above, online surveys were sent to 63 hospital site investigators. Of the 63 site investigators, 22 responded in the online survey.

Changes to manuscript: See above.

ii. Clear description of who did answer the survey would be nice.

Response: Thank you for this comment. Characteristics of the survey participants is provided on Page 11. In addition, we have added hospital size details.

Changes to manuscript:
Results section – Physician demographics

“Fourteen (45%) physicians who responded in the survey or interview were from small size hospitals (hospital size by patient recruitment <200 patients), followed by 26% from medium (201-500 patients), 19% from large (501-1000 patients) and 10% from extra-large (>1000 patients) size hospitals.”

b. Interviews: The title of the section is "Physician in-depth interview results: Implementation and acceptability of toolkit" yet, there are discussion of other components of the intervention.

Response: Thank you for this suggestion. We have revised the title of this section.

Changes to manuscript (Results section):

“Physician in-depth interview results and triangulation of ACS QUIK trial qualitative interview data”

i. Please review the number and description of who was interviewed in the results section? How many interviewees were from the same hospitals? I have put together that 28 interviews were from 27 hospitals, correct?

Response: Thank you. Yes, the reviewer is correct in that 28 physician interviews were conducted from 27 hospitals. We have clarified this in the Results section.

Changes to manuscript (Results section):

“We also interviewed 28 physicians (44%) from 27 hospitals who were selected from different cohorts with different hospital size and patient recruitment.”

ii. More quotes are needed in the different sections.

Response: Thank you for this comment. Given, our manuscript is already exceeding the prescribed word limit by the journal, we have provided more quotes in the Table 2.

Changes to manuscript (Table 2):

Refer Table 2 – illustrative quotes, under each theme: 4-5 quotes have been presented.
iii. It is not clear who used the toolkit components. The sentence on page 12 lines 22-27 is not concise. Who are the "physicians" - ED, cardiologist, general practitioners?

Response: Thank you for this comment. The toolkit intervention components were used by the quality improvement team, including physician, at each participating hospital. Physician site investigators were typically the chief of cardiology or chair of medicine who were interviewed in this process evaluation. Refer to page 12, lines: 16-18.

Changes to manuscript (Results section):

Online survey results

“ACS QUIK Toolkit intervention components were used by the quality improvement team, including physician, at each participating hospital.”

iv. Please describe exactly what the "Toolkit implementation score" is.

Response: Thank you for this comment. We have now provided a brief description of the “toolkit intervention implementation score” in the Methods section. The physicians from the hospitals who confirmed implementation of all four components, were assigned a score = 4, those implementing any three components of the toolkit were given a score = 3, those implementing any two components of the toolkit were given a score = 2, and those implementing one component of the toolkit were given a score = 1.

Changes to manuscript (Methods section):

“Physicians’ interview data, representing acceptability of toolkit intervention components (hospitals implementing all four toolkit intervention components were assigned a toolkit implementation score of 4, and those implementing any three, two or one toolkit intervention components, were assigned a score of 3, 2, and 1, respectively), were compared with changes in processes of care measures and clinical outcomes which occurred during the trial period.”

v. Audit and feedback reports were sent to "physicians" (page 13 line 26) what/who were these physicians? Are they the ones who were interviewed?

Response: Thank you for this comment. Yes, audit and feedback reports were sent to site investigators from each participating hospital on a monthly basis, and these were the same physicians whom we interviewed for the process evaluation.

Changes to manuscript (Methods section):
“Audit and feedback reports were sent via email to the physician site investigator from each participating hospital every month but were reviewed by a minority of physicians (example report in the Appendix).”

vi. More detail is needed to explain the statement on page 13 lines 29-36. I thought the purpose of the A&F was to help show whether or not the drugs were being utilized?

Response: Thank you for this comment. Audit and feedback reports provided more information than only what proportions of patients received recommended pharmacotherapy, including clinical outcomes, and time to diagnosis (ECG acquisition) and treatment (thrombolysis or primary percutaneous coronary intervention). A template of audit and feedback reports has been now added as online appendix.

Changes to manuscript (Methods and Appendix):

Audit and feedback template report added to the appendix.

“Audit and feedback reports were sent via email to the physician site investigator from each participating hospital every month but were reviewed by a minority of physicians (example report in the Appendix).”

vii. Page 14 line 26 - if junior physicians are reviewing the data - who are they reporting the findings to?

Response: Thank you for this comment. Junior physicians involved in the care of acute myocardial infarction patients themselves shared the information with the whole cardiology unit at the regular quality improvement team meetings.

Changes to manuscript: None.

viii. Checklists - those who had their own checklists, did you ask if they contained similar variables?

Response: Thank you for this comment. Yes, we did find out about the information included in checklists that some of the sites had their own. Most items on the checklists were similar as it was based on the recommended treatment guidelines. We did not capture the similarities and differences between trial and existing checklists.

Changes to manuscript: None.
ix. Please be consistent in statements. Page 14 line 50 "All physicians reported that checklists were considered important." Page 15 line 8 "Others reported that checklists made minimal difference in their clinical practice."

Response: Thank you for highlighting this. Actually, all physicians who were interviewed reported in principle that checklists were useful but there was heterogeneity in perceived value of the checklists. Some physician felt that checklists could be very useful for junior physicians. On the other hand, the highly trained and experienced cardiologists whom we interviewed felt that the checklists made minimal difference in their clinical practice.

Changes to manuscript (Results section):

“All (n=28) physicians reported that checklists were considered important for overall team performance.”

x. Guidelines for development and deployment of code and rapid response team: It is not clear in the Methods section page 7 lines 7-15 that "development and deployment of the code and rapid response teams" are part of the toolkit. It only states that there is access to the QI training.

Response: Thank you for this comment. We have provided specific details in the methods section that guidelines for the development and deployment of the code and rapid response teams were part of the toolkit (fourth component of the toolkit), and instruction on the potential value and methods for implementation were reviewed during the quality improvement toolkit intervention training sessions. The trial funding did not provide resources to provide this type of on-site training. However, high-quality cardiac arrest and rapid response teams have been widely recognized as important components for optimal in-hospital acute myocardial infarction care.

Changes to manuscript: None.

xi. Less useful section - Checklists - again, contradicts the statement on page 14 line 50 "All physicians reported that checklists were considered important."

Response: Please see our response to above response 8.b.ix.

Changes to manuscript: As above.
c. The "Intervention adaptation" is this more than the "toolkit"? More details of specific adaptation would be appreciated.

Response: Yes, intervention adaptation refers to the contextual modification made by the site teams (hospital staff including doctors, nurses) in the toolkit components. We have now highlighted specific examples to support this.

Changes to manuscript (Results section):

“For example, one site added details of the surgery or other intervention procedures performed in the discharge checklist. A few sites modified the patient education materials to include information on the starting dose and step-up dose of exercise post-discharge and dietary recommendations on salt intake.”

d. Page 16 and 17 under the discussion of payments: up to INR750/US$12 per participant - is this per patient or physician?

Response: INR 750 / US$12 was the payment given per patient to site investigators.

Changes to manuscript (Results section):

“Sites received payments for participation in the ACS QUIK trial (up to INR 750/US$12 per patient).”

e. Page 18 lines 29-34 "... trial participant satisfaction with the care provided..." How was participant satisfaction measured?

Response: Trial participant refers to the patients with acute myocardial infarction. Patient satisfaction was identified as a theme in the physician interview data analysis. Many physicians highlighted that their patients were satisfied with the care provided using the ACS QUIK toolkit intervention. No objective measures or treatment satisfaction questionnaire was used to assess patient satisfaction for the care they received during the trial.

Changes to manuscript (Results section): “Participant” changed to “patient”.

f. Page 18 lines 44-49 - please explain what this is talking about and why is this a barrier?

Response: We have revised the statement to improve the clarity of this statement. Barriers to implementation were related to changes in hospital staff, and internet connectivity problems. These have been described in Table 3 and supporting quotes have also been provided.
Changes to manuscript:

Deleted sentences:

“..slow decision-making for reperfusion from patients’ perspectives due to cost of treatment or approval sought from relatives,”

“Some physicians were not able to recognize the difference between a quality improvement implementation trial compared with a pharmaceutical company sponsored drug trial.”

Page 19 line 3 "Process evaluation - does that include both the survey and the interview? And "participants" are patients?

Response: Yes, process evaluation included both the survey and interviews. We have changed this to “implementation evaluation” to improve the clarity of this statement. Yes, participants refer to patients, and we have changed this wording.

Changes to manuscript (Results section): “Among ACS QUIK patients (n=12,686) enrolled by the 27 hospitals that participated in this mixed methods implementation evaluation, patients in the intervention phase…”

Please give more description of Table 4 on page 19.

Response: We have briefly summarized Table 4 in the manuscript.

Changes to manuscript (Results section):

“The key findings observed were improvements in processes of care measures, such as reperfusion among patients with ST-segment elevation myocardial infarction and prescription of in-hospital and discharge cardiovascular medications (aspirin, statins and blood pressure lowering agents) associated with the use of admission and discharge checklists.”

9. Discussion Section:

Page 20 lines 31-49 describes the formative evaluations and refers to the published manuscripts. Why did you not just refer to these in the methods section when describing the formative evaluation and tell us the findings that were used to modify the intervention?

Response: Thank you for this suggestion. We have removed the paragraph discussing findings from the formative qualitative work done to develop the toolkit intervention.
Changes to manuscript (Discussion section): Paragraph 2 removed.

b. Please clarify exactly what you are referring to in the statement on pages 20-21 lines 58-1-2. "Themes related to the strengths and weaknesses of the underlying mechanisms of the facilitation emerged with respect to catalyzing, doing, and reviewing."

Response: We hypothesize that the toolkit intervention led to integration of new activities that changed behaviour and performance through regular review. We have changed this sentence to be more explicit.

Changes to manuscript (Discussion section): “We identified themes related to the quality improvement toolkit intervention’s integration of new activities into existing activities that changed behavior and performance through regular review.”

c. Page 21 lines 21-37 may be used in the limitation section.

Response: Thank you for this suggestion. We have moved this paragraph under limitation section.

Changes to manuscript: Paragraph moved.

d. Results in on pages 21 lines 41-59 and the Context section are nicely done.

Response: Thank you for this comment.

Changes to manuscript: None.

Reviewer #2:

Overall comments: Thank you for an interesting paper that describes the journey of the ACS QUIK trial in Kerala India. It describes the development of a quality improvement intervention for the diagnosis and management of ACS trialled in 63 hospitals in Kerala, and the mixed methods process evaluation informed by the MRC process evaluation framework. I enjoyed reading the paper and appreciated the transparency and thoroughness of the methods and the findings, and the issues raised (in the discussion) about conducting such research in India resonated with me.
However, the paper was at times difficult to follow in some parts and I have some suggestions/clarification for your kind consideration. Overall, I think a tighter triangulation of your results and signposting your key findings would make your suggestions and conclusions in your discussion more apparent to the reader.

Specific comments for your consideration:

1. Minor comment, Abstract: There is slight disconnect between the focus of the abstract and the main text. For example, in the methods, the brief description of the development of the intervention was not included, and the conclusion of the abstract and main text in terms of considering the baseline quality of care of the hospital.

Response: Thank you for this comment. We have now added details of intervention development in the methods section and the consideration of locations/hospitals with low baseline quality of care for potential use of ACS QUIK toolkit to improve acute cardiovascular care in low-resource settings.

Changes to manuscript (Abstract section):

“Wider and longer-term use of the toolkit intervention and its expansion to potentially other cardiovascular conditions or other locations where the quality of care is not as high as in the ACS QUIK trial may be useful for improving acute cardiovascular care in Kerala and beyond”

2. Minor comment, Introduction: clear and presented the rationale for the study based on the data from the Kerala ACS registry. It may be helpful to include the potential relevance of your work to other hospitals in LMIC, i.e. in exploring whether implementing of guideline-based treatments shown to be effective in HIC, could be adapted in a LMIC setting given the contextual differences and challenges.

Response: Thank you for this insightful comment. We have included this in the background section.

Changes to manuscript (Background section):

“This has relevance for potential adaptation of the ACS QUIK toolkit intervention in other low-resource settings as well, given the contextual differences and challenges in implementing the guideline-based treatments shown to be effective in high-income country settings.”
3. Minor comment- Methods: As your methods span 2012 till 2016- It may be helpful to include a succinct timeline of when each part was done to enhance the readability.

Response: Thank you for this comment. We have provided specific details on the timeline for each activity in the methods section to improve readability.

Changes to manuscript:

Methods section - Overview

“This mixed methods study included pre-trial toolkit intervention development (March 2011) using semi-structured interviews and focus group discussions and within-trial online survey data and semi-structured interviews with physicians (November 2015 – December 2016) involved in the ACS QUIK trial”.

4. Major and minor comments- Results: Overall, this section was at times difficult to follow.

a. Online survey, I would suggest condensing this by only referring onto the tables, and summarising the key points from the survey. E.g. the low implementation of the establishing the code blue team.

Response: Thank you for this comment. We have tried to balance this reviewer’s comment with Reviewer 1’s comments, who called for additional quotations to support our conclusions.

Changes to manuscript (Results section): We have cut 1 of 3 quotes from theme 4 as recommended below by Reviewer 2.

b. Physician in-depth interview results: Suggest leaving the overall summary for the discussion and present the 4 themes directly. I liked Table 2 with its illustrative quotes. For consistency and to enhance readability, I would suggest that for theme 4: recommendations, that you include less direct quotes.

Response: Thank you for this suggestion. We have removed the overall summary and presented only four themes directly in the results section. We have also removed 1 of 3 quotes for theme 4 as recommended.

Changes to manuscript (Results section): We have cut 1 of 3 quotes from theme 4 as recommended below by Reviewer 2.
c. Facilitators and barriers: There seemed to be some overlap with the previous section. (i.e. Physician in-depth interview results: implementation and acceptability of the toolkit). I wonder if it would be possible to merge these findings (e.g. facilitator of physicians believed in the toolkit, and usefulness of checklist fits with your first theme of usefulness/acceptability of the ACS QUIK toolkit). And to expand on your interpretation in the text.

Response: We agree there is some overlap but less so in terms of barriers to implementation, which we have tried to address in this brief section. We have cut several lines in this section to shorten it further to address this reviewer’s concerns.

Changes to manuscript (Results section): Paragraph shortened.

It may also help to split them to individual, organisational and policy level barriers or just across the components.

Response: Thank you for this comment. We have grouped the barriers summarized in Table 3 under the sub-headings: individual and organization level. We did not explore policy barriers in this implementation evaluation, though this has been part of previous, related work within our study team related to policies related to pre-hospital emergency care.


Changes to manuscript: Table 3 updated with the recommended headings.

d. Integrating results of the process evaluation with ACS QUIK trial outcomes- pg 19 ln 41-54. Could you clarify whether you are triangulating your findings with the ACS QUIK trial results? (In 49 seems to suggest you are not?) pg 19 ln 24-34.- this link between the use of the tool kit components and the rates of process measures seems to be one of your key findings but could be emphasized more clearly either in the main text of in Table 4.

Response: Yes, we have triangulated the results from implementation evaluation with the ACS QUIK trial main findings. We have highlighted the key findings of the triangulation in the results section in Table 4.

Changes to manuscript:

Results section, Table 4

“The key findings observed were improvements in processes of care measures, such as reperfusion among patients with ST-segment elevation myocardial infarction and prescription of
in-hospital and discharge cardiovascular medications (aspirin, statins and blood pressure lowering agents) associated with the use of admission and discharge checklists.”

5. Minor and major comments, Discussion: I found this interesting and insightful, but have some further areas for clarification.

a. Summary: pg 20 ln20- the statement 'a relatively high-level of care at baseline in the control group hospitals' was not apparent to me from the findings.

Response: Thank you for this comment. We have added a brief example of high-quality care based on discharge aspirin rates to help demonstrate this.

Changes to manuscript (Discussion section): “However, a relatively high-level of care at baseline in the control group hospitals (e.g. >95% rate of discharge aspirin use)…”

b. 'favourable temporal trend'- what does this mean?

Response: ‘Favorable temporal trend’ refers to the background improvements in clinical care observed over the study period.

Changes to manuscript (Discussion section):

“…favorable temporal trends (i.e. background improvements in clinical care over the study period) limited the effect of the toolkit intervention on clinical outcomes.”

c. Pg 20 ln 32-49: I liked this paragraph but it does not seem to be natural fit under 'summary of findings' and access to life-saving reperfusion therapy was not clearly mentioned in your results. Is the 'formative qualitative evaluation' part of the focus groups in your development of the intervention, if so, perhaps some of these findings i.e. ln 39-49 could be in your results.

Response: Thanks for this comment. We have now removed this paragraph from the discussion section.

Changes to manuscript: Paragraph removed.

d. Explanation of results: ln pg 21 ln 2-3, 'catalysing, doing and reviewing' in this relation to the physicians' work or the researchers. It is not clear to me what this meant.
Response: See response to Reviewer 1’s comment related to this point.

Changes to manuscript: See above.

e. Pg 21 LIn 21-36: seems to fit better under the strengths and limitations of the study. Could you comment in line with this, whether there is a role of follow up interviews etc. after knowing the results of the trial outcomes?

Response: We have moved this paragraph to the strengths and limitations section and also commented on the implications or role of follow-up interviews after knowing the results of the trial outcomes.

Changes to manuscript: Paragraph moved.

f. Pg 21 LIn 41: This paragraph about implications i.e. about the need for 'concurrent investigation in improving the structural capacity of hospitals' seemed to be the take-home message to me for future work in this area. However, the results do not clearly point to this implication. Could you comment on with the benefit of hindsight, how this could have been further investigated or potentially accounted for during the set-up of the trial in terms of variation of the ACS QUIK trial hospitals?

Response: Some of these conclusions are grounded in our observations, prior research, including the Health Care Provider Performance Review published by Rowe et al. (Lancet Global Health 2018; 6(11):e1163-e1175), as well as our team’s follow-up yet-to-published research using an adapted version of the World Management Survey to evaluate management practices in participating hospitals. We have added the Rowe reference, which is particularly strong in placing interventions like ours into context.

Changes to manuscript: Rowe et al. reference added.

g. In line, with this- could you comment on the potential next steps for this network of hospitals? For example, the sustainability of the intervention, or components of it e.g. educational materials, which maybe more readily embedded into the system?

Response: The ACS QUIK network of hospitals and its infrastructure have served as a platform for research trainees and junior investigators who have collaborated with the investigators from the Cardiological Society of India, Centre for Chronic Disease Control, and Northwestern University. For example, this network of hospitals was utilized in our subsequent evaluation of management performance using an adaptation of the World Management Survey, and we found
that managers had relatively weak goal setting performance, suggesting that sites may have had a
difficult time taking data from the hospital audit and feedback and incorporating that into a
monthly or quarterly goal with a corresponding plan on action (unpublished data). Further, our
study team is exploring management-level interventions to improve acute care quality and safety
while also evaluating potential methods for simulation-based quality improvement training.

We recognize that ACS QUIK toolkit could be expanded to other states in India and
countries in South Asia as well as other acute cardiovascular conditions, including stroke and
heart failure, the latter which we have begun to evaluate in pilot testing in Kerala. We are also
interested in streamlining the data capture, cleaning, and feedback process to target key
structural, process, and outcomes measures. We are exploring partnership with the national
Cardiological Society of India to adapt the intervention in settings with lower quality baseline
acute myocardial infarction care and worse outcomes than Kerala, which now experiences
survival rates that are similar to those in the United States. Much of this information falls
outside the scope of this manuscript, especially given its current length. We have tried to address
many of these topics briefly and generally related to other settings and other conditions where
the intervention might be effective, which is supported by the aforementioned Health Care
Provider Performance Review.

Changes to manuscript (Discussion section): Rowe et al. reference added.

h. Results in context: suggest tightening these paragraphs for to enhance the readability of the
   paper.

   Response: As per the reviewer’s recommendation, we have shortened this section.

   Changes to manuscript (Discussion section): Section shortened.

i. Strengths and limitations: pg 24 ln 2, this does not seem to be a limitation of the study.

   Response: Thank you. We agree with the reviewer suggestion and have deleted this from the
   limitation section.

   Changes to manuscript (Discussion section): Limitation deleted.

j. Pg 24 ln 24: could you comment on your reasons for not sampling across health provider
   roles?
Response: We interviewed the lead site investigator (physician) from the participating hospitals in ACS QUIK trial because they were primarily responsible to oversee the implementation of the ACS QUIK toolkit intervention. Although it would have been informative to interview participants across health provider roles, we only invited the site investigator based on study budget and feasibility. We acknowledge this as a limitation.

Changes to manuscript: None.

k. Pg 24 ln 27-21: this statement is not clear to me.

Response: The last statement under the limitations section. “Lastly, there could be potential confounding between sites, site investigators, toolkit implementation, and clinical outcomes, which are difficult to quantify or control” refers to the potential confounding (unknown confounders at the hospital level or providers characteristics, influencing level of toolkit implementation and hence, the clinical outcomes) leading to variability in trial outcomes across non-randomized groups. For example, high implementing hospitals may behave differently (and may have different patient groups) than low implementing hospitals, which might drive process of care measures and outcomes.

Changes to manuscript (Discussion section): “unmeasured” added to this sentence.

1. Conclusions: pg 24 ln 51: 'quality of care of the ACS QUIK hospitals'- could this be more explicit in the results? As it reads currently, the variation in quality of care of the hospitals is not apparent to me.

Response: Thank you for this comment. We have now highlighted the quality of care of the ACS QUIK hospitals in the results section under Table 4 and supplementary results.

Changes to manuscript: Table 4 updated.

6. List of Tables and Figures:

a. Table 1: overall clear. Clarification- Is the online survey of N=22 from 22 different hospitals?

Response: Yes, we have added the units to Table 1.

Changes to manuscript: “Hospitals” added to Table 1.
b. Overall, I think Table 2 and 3 could potentially be merged together. Or perhaps move one or the other as supplementary tables.

Response: These tables are relatively long, which argues against merging them, and they build upon each other to help set the reader up for the synthesis of results in Table 4. We prefer to keep the tables in their current form but can discuss further with the editors if they feel strongly about this point.

Changes to manuscript: None.

c. Table 2: I like the illustrative quotes.

Response: Thank you.

Changes to manuscript: None.

d. Table 3: I like your statements on 'context, conditions and consequences.'

Response: Thank you.

Changes to manuscript: None.

e. Table 4: I do not understand the outcome: observed, implied or anticipated… what does this mean? I think incorporating the contextual barriers may be helpful in helping explain your outcomes.

Response: Table 4 outcomes are based on the triangulated results from the survey and interview data. Thus, we categorized the outcomes into observed (directly evident from the data), implied (no direct data available but interpreted based on triangulated results), or anticipated (based on assumptions guided by the interview or survey data). We have clarified this in the Table legend.

Changes to manuscript: Table 4 legend updated.

f. Figure 1: a nice diagram to summarise the formative work. It may be helpful to elaborate briefly in the main text why the phrases in red were identified as the potential targets. Was this through consensus in the focus groups?

Response: Thank you. This was through expert consultation among the study team and site investigators based on what seemed feasible based on interventions and their known effects.
Changes to manuscript (Results section): “The framework method[11] was used to create a contextualized critical pathway for patients with acute myocardial infarction with opportunities for intervention highlighted (Figure 1).”

g. Figure 2: I think this summarises table 3 quite nicely but the adaptation and sustainability boxes could be improved with further headings perhaps of the individual components.

Response: We have updated Figure 2 to try and provide greater clarity about adaptation (by adding further headings of the individual components) and sustainability (summarize the points suggested by the physicians to improve scale-up of toolkit intervention components).

Changes to manuscript: Figure 2 updated.

h. Thank you again for all your work in this area. It was great to read about the formative work and the in-depth mixed methods process evaluation in the area of quality improvement in such an important area of need. All the best.

Response: Many thanks for all your very helpful comments, queries and suggestions.

Changes to manuscript: None.