Author's response to reviews

Title: Quality indicators in continuous renal replacement therapy (CRRT) care in critically ill patients: protocol for a systematic review

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Author's response to reviews: see over
Dear Editorial Team,

Re: MS: 1006315309158536 resubmission titled: Quality indicators in continuous renal replacement therapy (CRRT) care in critically ill patients: protocol for a systematic review

We are grateful for the opportunity to revise and resubmit our manuscript. We have reviewed your letter dated April 7, 2015 and provided an itemized summary of responses to the Editor and Reviewer comments below.

In addition, as recommended, we have updated our search strategy, now included as “Figure 1. Search Strategy_revised.” In addition, we have added another contributing author to our study. Finally an appendix with the PRISMA-P checklist has been added as “Appendix 1.”

We believe our protocol has been strengthened in response to the Editor and Reviewer comments.

We hope you now find our manuscript suitable for publication in Systematic Reviews. If there additional questions or queries, please contact us at your convenience.

Kind Regards,

Sean M Bagshaw
Oleksa Rewa

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May 6th 2015
Response to Handling Editor’s Comments:
1. The authors should be encouraged to cross-check their protocol against PRISMA-P as some reporting items appear missing and it would preferred if a complete checklist could be submitted.

   Thank you for this good point. We have now included the PRISMA-P checklist as an appendix to the study as “Appendix 1.”

   The protocol has been amended on page 6 to read:

   “We will perform a systematic review to identify and evaluate QIs for the prescription, delivery, monitoring and outcomes for critically ill patients receiving CRRT using the guidelines from Cochrane and Center for Reviews and Dissemination and as described according to the PRISMA-P guideline (Appendix 1).”

   Additionally the text has been modified as to read as follows:
   Page 13: “Baxter Inc. has had no role in the development or preparation of this protocol.”
   Page 13: “SMB will guarantee the content of the review.”

2. PROSPERO describes the comparator for these QI studies to be usual care, this is not mentioned in the protocol and should be included. This needs clarification as the study designs included are not restricted and so a usual care comparator will of course not always apply. Does this mean that reports comparing two QIs will be excluded? If so, this needs to be explicitly reported."

   Thank you for bringing this to our attention. We are not necessarily evaluating the comparative aspect of these QIs at this stage. Rather, we are more focused on their identification. We have now clarified the inclusion criteria section of page 7 to read:

   “These studies will not be limited to comparative studies and will include any literature with mention of QIs.”

Response to Editorial Comments:
1. Please include a list of abbreviations used in the manuscript and their meanings.

   Thank you. These have now been added to page 1 of the manuscript and reads as follows:

   “Abbreviations: ICU – intensive care unit; RRT – renal replacement therapy; CRRT – continuous renal replacement therapy; QI – quality indicator”

Response to Reviewer Comments

1. The authors list 9 themes that will be used to group the various quality indicators that might be used for CRRT. The breadth of these themes means that the review will cover a very extensive list of potential interventions in the review. It is difficult to see how many of these themes would relate to the quality of CRRT. For example, the authors list high versus low dose prescription of drugs as a quality indicator. The current protocol does not explain how this would indicate the quality of the CRRT. The same criticism applies to each of the themes and all of the potential quality indicators within each theme.
We appreciate the Reviewer’s comment. We agree – our review may indeed find a large number of potential quality indicators for CRRT. The themes we have listed in the table represent potential areas where we believe a quality measure could be developed for the prescription and/or delivery of CRRT. Where there is no validated evidence-informed quality measure and where there is the perception among providers that a quality measure within a specific theme may have value, future work would be aimed at developing one. Additionally, after our initial review of the literature search, we have determined that drug monitoring will not serve as an appropriate surrogate of quality of CRRT delivery. Rather, this theme will be encompassed in the dose prescription and delivery theme of CRRT. Accordingly, we have removed this theme from our inclusion criteria and the manuscript has been amended accordingly as has Table 1. We have revised our manuscript on page 7 to read as follows: “An initial screening of retrieved literature considered drug monitoring and drug levels as a potential QI; however upon further review this was deemed not to relate to a QI in CRRT and has been removed drug monitoring as an inclusion theme.”

2. The main weakness of the protocol as written is the lack of an outline on how the quality indicators will be assessed for their impact on clinical outcomes, for example survival of the patient and reduction of complications. The protocol states that “Scientific acceptability will assess how plausible each QI measures respective outcomes”. The lack of a method to assess the impact of the quality indicators on outcomes of significance to patients needs to be rectified. The types of outcomes that will be assessed needs to be considered and discussed.

We appreciate the Reviewer’s comment. We agree with the Reviewer. We recognize we have not specifically detailed how each quality measure will be evaluated against a patient-centered outcome. This stems from i) we are uncertain of how many potential quality measures will be found by our systematic search; ii) not all quality measures will necessary correlated directly with high-level patient centered outcomes (i.e., survival) – many will focus on ensuring “value for money” and be resource or economic in nature. However, in studies were an association between a quality measure and a patient centered outcome is described – we aim to include this in our evaluation. Where this does not exist – we will recognize this as a knowledge gap – and aim to specifically validate this association in the future. We have revised our protocol manuscript on page 9/10 to read as follows: “Candidate QIs will be each evaluated for their operational characteristics including association with circuit lifespan, resource intensity (i.e., nursing workload) and health care costs, as well as for their potential to be integrated into electronic medical records, if applicable.”

3. The inclusion/exclusion criteria are not well outlined as several of the outcomes (eg feasibility) being considered would not necessarily be studied in the type of intervention studies outlined, and are more likely to be studied in qualitative or mixed methods studies. On the other hand, using case-control studies and case series data to assess the effectiveness of the indicators is likely to result in a high risk of bias.

We appreciate the Reviewer’s comment. We have clarified our inclusion/exclusion criteria on page 6 to read as follows: “6) Levels of evidence, all primary studies (i.e., randomized control trials, cohort studies, case-control studies, case series and qualitative or mixed methods studies), secondary analyses or evidence syntheses (i.e., systematic reviews, meta-analyses and Cochrane reviews), as well as targeted grey literature including technical reports from industry or to governments or health care agencies.” We believe this importantly reflects that i) no evaluation of this nature has been performed to
date; and ii) there is uncertainty regarding the anticipated search results; such that we have specifically been conservative in our approach.

The definition of outcomes have been revised to include further evaluation that will occur in the second phase of this project after the initial identification of candidate QIs (the primary purpose of this systematic review). The manuscript has been revised to include this on page 9 as follows: “These outcomes will be further evaluated in the second phase of this project when candidate QIs will be evaluated and ranked by knowledge users, stakeholders and experts.”

We have also addressed limitations to these outcomes on page 12 to read as follows: “We will utilize the NOS or COSMIN checklist to quantify and evaluate the risk of bias across studies and these measures will be included in our analysis.”

The risk of bias in the studies will be evaluated as per point 4 below.

4. The authors do not report how they will assess the risk of bias of the studies to be included in the review or how quantitative results will be combined where available.

Thank you for bringing this to our attention. We have clarified that we intend to use of two tools for the assessment of this bias (Newcastle-Ottawa Score and COSMIN checklist) in our study. The protocol has been updated on page 9 to read as follows: “Methodological quality will be rated using the Newcastle-Ottawa Quality Assessment Scale (NOS) for observational studies and a modified version of BOAS for before-after studies, as applicable. Qualitative studies will be evaluated using the COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN checklist) with four point scale.”

5. The search appears well considered and appropriate. However, the limiting of studies to particular languages is a potential bias of the review.

Thank you for bringing to light this valid concern. In the current protocol, we are reviewing data in English, French, German, Italian and Spanish. These languages were selected as the majority of high quality data in critical care are published in these languages. While there may be certain studies published in other languages, the quality of this data at times comes into question, and may not be appropriate for inclusion in our study. Additionally, due to technical and feasibility concerns, we must limit our inclusion to these five languages. While we recognize that this may represent a potential source of bias in our search strategy, we do not believe this will translate into a significant loss of information. The manuscript has now been amended in the Limitations sections on page 12 to read: “As well, we have limited our search strategy to include only studies in English, French, German, Italian and Spanish. We recognize this may result in studies that describe potential QIs for CRRT being omitted; however, we believe this languages will represent the majority of high-quality published research in critical care.”