Author's response to reviews

Title: Evaluating processes of care and outcomes of children in Hospital (EPOCH): Protocol of a multi-center cluster randomized trial

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Version: 2
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Author's response to reviews: see over
Author's covering letter for initial submission

Title: Evaluating processes of care and outcomes of children in Hospital (EPOCH): Protocol of a multi-center cluster randomized trial

Authors:

Version: Date: 11 February 2015

Comments:


The authors wish to thank the reviewers for their thoughtful and constructive reviews, and the editors at TRIALS for the opportunity to respond. Please find the below our point-by-point responses to the reviewers and editors itemized comments and suggestions.

Reviewer 1.

GENERAL

The manuscript describes in detail the process of developing a large clinical trial to evaluate the efficacy of utilizing an early response team for preventing cardiac arrest and complications in hospitalized pediatric patients. The project is quite ambitious seeking to enroll 100,000 patients hospitalized for 400,000 patient-days in 22 hospitals utilizing a cluster design.

This is an important work for those who wish to perform studies like this and for those who will be interested in evaluating this study when it is complete.

It is very detailed and complete.

MAJOR REVISIONS: none

MINOR REVISIONS:

The authors flip flop back and forth using the proper pleural form for the word "data" which is pleural and improper form, the singular. For example, it is used properly as the pleural form in the CONFLICT of INTEREST section, 4th paragraph, line 7, .."data are correct..." and LIMITATIONS of EPOCH, paragraph lines 10-11"...acquisition of these data for...." However, it is used improperly in several other places,

1), Sample Size and assumptions, para 2, line 1; Data from 4 paediatric hospitals in Ontario indicates...." (should be indicate),

2). Results, para 2, line 2, "....data is..." (should be data are).

Thank you this has been corrected.
3. Conflict of Interest, para 6, line 1, "...the data and its..." (should be the data and their).

4). Discussion, para 1, line 1,"...Preliminary data suggests that..." (should be Preliminary data suggest that) PLEASE BE BOTH CORRECT AND CONSISTENT.

Authors: Thank you. These variations have been corrected in the revised manuscript.

DISCRETIONARY REVISIONS: Although I think I understand the reason for this, the Tables are unusual. They look more like the information usually presented in an appendix. Please look at this and think about if there is a better way to present the information.

Thank you. We agree that some or all of these tables could be included as appendices. We leave this to the discretion of the editors.

Level of interest: An article of importance in its field

Reviewer's report
Title: Evaluating processes of care and outcomes of children in Hospital (EPOCH): Protocol of a multi-center cluster randomized trial
Version:1 Date:8 November 2014
Reviewer: Patrick Brady
Reviewer's report:
Major comments:
1. This is very important and well-thought out study with great implications for the safety of care delivered to hospitalized children. The protocol would be a valuable addition to the fields of critical care, hospital medicine, and safety.

Authors: The authors thank the reviewer for this comment.

2. Please be clearer on how the participating hospitals were identified/recruited. I could not find this anywhere in the protocol, and if this were a process where hospitals could self-select due to interest in BPEWS, this may over-state (or under-state) the effect size of BedsidePEWS.

Authors: The text has been modified to better explain this point. Page 21 ‘Planned conduct’ “Hospital recruitment though the networks of the CCCTG preceded the enrolment of hospitals with an identified site investigator, administrative and research ethics board approval, and was contingent on the number of sites previously enrolled in the study.”

3. While most of the paper is quite well-written I felt the introduction was rather uneven. I'd ask the author group to consider framing this is the context of rapid
response systems with afferent limbs (of which BPEWS is a robust and well-validated example) and efferent limbs that would include some of the recommendations from BPEWS and METs. I think the statement that "MET-RRT have not fulfilled their promise," but I was bothered that two systematic reviews of pediatric RRTs showing decreased mortality were not referenced. I agree this literature is not perfect, but a mortality benefit in systematic reviews needs to be acknowledged.

Authors: As recommended, the introduction has been edited to reflect afferent and efferent limbs of the system, and the systematic reviews referred to have now been referenced for the interested reader (REF: 41). Note that the systematic review of RRT in Annals of Internal Medicine includes no randomized trials, and is largely influenced by the two studies that we describe in detail from RCH Melbourne and Stanford group. The summary from the systematic review was that ‘robust evidence to support their effectiveness in reducing hospital mortality is lacking’. This proposed RCT will directly address this recommendation.

4. Another issue with the MERIT study was that several of the "control" hospitals implemented some kind of MET during the study period, biasing it towards the null. The authors were clear on hospitals agreeing not to use an EWS if assigned to control, but they should be clearer on what if anything was to be done with METs.

Authors: As recommended, the handling of hospitals (in the EPOCH trial) with MET teams (or those planning to start or stop a MET-RRT) has now been clarified and emphasized in discussion section, complimenting the text describing our exclusion criteria. “To ensure that major system changes do not introduce bias we will exclude hospitals that plan to introduce or discontinue a MET-RRT during the study, are already using a severity of illness score in wards, or consider randomization unacceptable. Hospitals with a pre-existing MET-RRT are eligible to participate.”

5. The conflict of interest section of this protocol and of the study overall were quite well done, and I appreciate that the author has acknowledged and that this group continues to contribute to scientific knowledge and describe their methods. I, however, am unclear what difference if any there is between what they were testing and the product of Bedside Clinical Systems. If this is the exact product please state that clearly.

Authors: The text has been modified to explicitly state the products of the company include the BedsidePEWS. “BedsidePEWS is an FDA approved product of Bedside Clinical Systems. The study PI (CSP) is a named inventor of the BedsidePEWS (US patent 12/669,896). The patent is owned by the host institution (SickKids).”

6. Related to this I think it would be both better for readers and better writing if
the lead author would acknowledge that he developed the BedsidePEWS; it
seemed odd to the this section in the third-person when most of the references
were to papers by Dr. Parshuram.

Authors: As recommended, this now is addressed and explicitly acknowledged
(please see the above section).

Minor comments:

1. I did not understand the rationale behind the survey of decision makers. Could
you please explain this briefly? The other outcomes assessed are so robust that
I'm not sure why the CEO's thoughts have particular scientific validity if they
disagree with outcome and process of care measures.

Authors: This component of the study relates to the process of this type of
research, and the experiences of the Decision-makers who in essence provided
the ‘consent’ of the institution. The text has been modified to better explain this
point (Page 16). “to describe the experience of the decision-maker in
participating in a hospital-wide cluster RCT, and their expectations of its results.”
Thank you.

2. The tables are generally useful but consider if CRI scale which you've
published elsewhere could be referenced and the surveys included instead. I
appreciate the counterargument that the CRI is more central here.

Authors: Thank you. The Surveys are included in the Appendix CRF. We prefer
to include the tables, but defer to the editors on this point.

3. Even if you do not choose to include the surveys please comment briefly on
how they were developed and any evidence of their validity and reliability.

Authors: Thank you. The surveys are included in the CRF appendix. Additional
text has been added to clarify their development, validity and reliability (Page16,
Paragraph 1). The decision-maker survey was purpose-built and the
documentation and interaction survey was developed by our team and has been
used in our previous evaluations. “ This custom-built survey was developed and
used in our pilot evaluations of BedsidePEWS. It has not been formally
validated.”

4. I'm not sure if this has to do with IP, but it would be quite valuable to see what
guidance the BPEWS provides in the event of certain scores (are they related to
mandatory ICU consults, increased VS, contact with members of the primary
team). I could not find this in other papers nor how the process worked with the
280 doctors that helped shape these. The high number is a strength but I wonder
how this worked since they probably couldn't talk back and forth on the strengths
and weaknesses of strategies at different scores.

Authors: These recommendations are customized for each hospital. Additional
text has been added to better describe the nature of the recommendations. Page
13 section: Intervention: BedsidePEWS. “…in each of the domains of vital sign
assessment, secondary review, continuous monitoring, and ICU consultation, and customized for each implementation.”

5. In the first paragraph of the methods it states "more than 200 inpatient admissions in eligible inpatient wards" Should this be eligible admissions or pediatric admissions or are these all children's hospitals?

Authors: The 200 refers to all paediatric admissions receiving care in the inpatient wards. The text has been modified to better reflect this point. “…more than a total of 200 eligible inpatient admissions in eligible inpatient wards each year”

6. The table with the measure definitions is generally quite well done, but there are two measures I still fail to understand. Urgent PICU admission seems to be arriving in the PICU within 6 hours of decision to admit. Why is this important? This seems at least as much about PICU bed availability as it is child’s status, at least when it comes to the difference between 5 hours and 6.5 hours.

Authors: Thank you, the decision to characterize urgent ICU admission as admission within 6 hours of the decision to admit reflects the operationalization of ‘urgent’. This was a pragmatic, consensus decision after long discussion among the steering committee experts and the Canadian Critical Care Trials Group, at large.

In PRISM / PICUES this is a 12 hour window. One could argue that all admissions to ICU are planned – that the distinguishing features are the time between the decision to admit and the admission to ICU. This threshold in some systems is 6 hours and in other systems is 12 hours. For our study we chose the shorter, more conservative time period of 6 hours based on discussion and the collective judgments of the clinical experts in the steering committee and the Canadian Critical Care Trials group. Moreover our experience would suggest the majority of children who are urgently admitted from a ward to an ICU bed, tend to be moved considerably more quickly than 6 hours. Additional text has now been added to clarify this pragmatic/practical design choice in the secondary outcomes clinical section (page 15, paragraph 1): “Urgent PICU admission is defined as departure from the inpatient ward within six hours of the decision to admit to ICU (Table 2). This definition reflects the need to pragmatically distinguish between urgent and elective admission the experience recognition that most urgent admission occur within 1-2 hours of the decision to transfer to ICU.”

7. I also don’t understand how 'stat' calls were operationalized/measured in a multisite fashion. The concept makes sense but I imagine the scenarios that a nurse would call for 'stat' would vary from hospital to hospital and nurse to nurse.

Authors: Thank you. We have clarified this in the text (page 15 Secondary outcome process of care). “This was formally defined (table 3) and a consistent approach to data collection was applied throughout the study, recognizing that cultural and other factors may contribute to considerable inter-hospital variability.”
Smaller comments not for publication:
1. BedsidePEWS is at times written BedsidePEWS, Bedside PEWS and Bedside-PEWS. Please be consistent.
Authors: Thank you, these variations have been rendered consistent.
2. In table 3 and throughout paper, please change unplanned readmission and unplanned PICU readmission within 48 hours as to "within 2 days." It’s no validity threat that you measure this in days at 3rd midnight but writing it as hours is a bit misleading.
Authors: Thank you. This has been modified.
3. There are a number of occasions where the future tense is used. This read oddly since the study is underway.
Authors: Thank you. This has been revised.
4. Table 4, row 6 needs stretched out a bit.
Authors: This has been done in the submitted word file. Subsequent modifications may occur at the copy editing stage.
5. Enrollment is misspelled in row 5 of table 6.
Authors: Thank you. This has been rectified.

Level of interest: An article of outstanding merit and interest in its field
Quality of written English: Needs some language corrections before being published
Statistical review: Yes, and I have assessed the statistics in my report.
Declaration of competing interests:
I have no competing financial interests. I have performed work on a different Pediatric Early Warning Score which was recently published.

Editorial requests:
1. Please include the email addresses of all authors on the title page.
Authors: Thank you. The email addresses have been added. The CCCTG is a national body, so an person-specific email has not been provided.
2. The title page should include the title of the manuscript, the names, affiliations and email addresses of all authors, and the corresponding author should be indicated. Please remove all additional information.
Authors: The title page has been revised. Thank you.

3. Please restructure the Abstract. The Abstract should be composed of the following four sections: Background, Method, Results and Conclusion and should be no longer than 350 words. Please include the trial registration number and date of registration at the end of the Abstract.

Authors: The abstract has been reformatted to match the above, with description of the trial status in the results section.

4. Please rename the Introduction section, 'Background'.

Authors: Thank you. This is done in the revised manuscript.

5. Please include the names of all ethical bodies that approved your study in the various centres involved, along with the reference numbers given, in the Methods section. If you do not wish to list them all in the Methods section, please include the list as an additional file and refer to this in the methods section.

Authors: The list will be provide as a separate file and has been referenced as Appendix 1: ‘The enrolled sites and associated ethical approvals are provided in Appendix 1.” Please see attached.

6. Please include a list of abbreviations used and their meanings, after the Conclusions section.

Authors: This list has been added as described.

7. Please rename the Contributors section ‘Authors' Contributions'.

Authors: Thank you. This is has been done in the revised manuscript.

8. Please mention each author individually in your Authors' Contributions section. We suggest the following kind of format. (description removed for brevity).

Authors: Thank you. This is has been done in the revised manuscript.

The authors thank the editors for the opportunity to respond, and look forward to our future correspondence.

Sincerely

C Parshuram

for the authors