Author’s response to reviews

Title: A feasibility study of a randomised controlled trial to examine the impact of the ABCDE bundle on quality of life in ICU survivors

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Author’s response to reviews:

Dear Editor and Reviewers,

We appreciate your feedback and suggestions regarding our previously submitted manuscript. We have responded to each of your comments below and have made suggested track changes to the manuscript.

Kind Regards

Kellie Sosnowski

Reviewer # 1

1. In the section "Intervention group", the authors describe the specific components of the ABCDE bundle and that education on the bundle commenced two months prior to study commencement.

Given the this is a single site study and the clinicians/nurses were likely treating both intervention and control patients, were you able to compare receipt of the bundle elements in
both the intervention and control groups? i.e. how much spill-over occurred into the control group due to the fact that the clinical team were using this care bundle on the intervention patients?

It would be great to see these data reported.

Author's response:

As this was a proof of concept trial, we were keen to see if we could deliver this complex intervention.

The following text regarding the minimization of contamination of the care of the control group is included in the Discussion section.

Line 512 - 522

“Potential contamination of the care of the control group was considered. The intervention group received the standardised and protocolised ABCDE bundle via a prescription within the clinical information system which once ordered could not be ignored or deleted resulting in the delivery of consistent and standard care every day. To provide additional control in our pilot study, only the intervention group had access to the ABCDE protocols via the clinical information system. The protocols were not available in any other format. Alternatively, the control group received care dependent on the medical officers, physiotherapists, occupational therapist, nursing decisions made daily with no use of protocol.” Variation in the control group occurred related to different clinical practice and effort of individuals.

In addition, the following text has been included within the limitation section.

Line 532 - 534

“It is possible that some clinicians would have provided the intervention to all patients. A future RCT would benefit from the inclusion of data related to potential contamination of the control group.”

2. Along the lines of comment 1), it would be great to see a discussion of whether the authors feel that the best design for a controlled trial of the ABCDE bundle is randomization of patients within units vs. the more traditional approach of a cluster randomized trial. Can the authors provide justification for why they decided to randomize within the single site and also, give a recommendation of how they would see a larger, sufficiently powered RCT implemented.

Author's response:

We are mindful that this is a complex intervention, and were keen to provide proof of concept prior to embarking on a multi-site trial.
We have successfully tested our procedures in this feasibility study and are confident we have designed a rigorous single-centre RCT. Our plan is to ultimately progress to a well-designed multi-centre phase III trial, and the use of a cluster randomized trial is well worth considering.

However, our plan is to now perform a single site randomised controlled trial to test our hypothesis for the following reasons:

- Costs of the trial will be minimised. We can finance the trial with small grants only, whilst additional human and physical resources will be supplied from within our ICU labour and non-labour budget.

- The research team will be very available and involved throughout. We found our level of continual enthusiasm very helpful to continually drive this complex intervention out on the patient floor.

- We can easily coordinate all trial activities.

The future RCT will ensure that a multi-site trial is warranted and that the study design is efficient and robust.

3. Although the authors are correct in not reporting results of statistical hypothesis tests within this feasibility study, it would be interesting for the authors to comment on the observed size of the mean outcomes across the intervention and control groups; i.e. are the means in the appropriate direction as you would expect given the goals of the bundle?

Author's response: We believe the results related to ICU stay were skewed by the participants suffering from gastrointestinal disorders. The following text has been added:

Line 346 - 349

“All four patients admitted with gastrointestinal disorders were randomised to the intervention group. This may have skewed results as they had a lengthy ICU stay (Mean 16.2 days SD 11.6) and lengthy duration of ventilation (Mean 14.1 days SD 11.3).”

The following text discusses better functional and quality of life results in the intervention group

Line 415 - 418

“Despite longer length of stay and duration of ventilation, intervention group mean scores indicated better functional and quality of life results at discharge. However, the sample size was too small to provide reliable interpretation.

Reviewer # 2
1. I believe the pre-specified definition of trial success should be stated in the abstract. It is some way in to the manuscript before these are listed.

Author's response: Thank-you for your suggestions. The following text has been added to the objective section of the abstract as advised.

Line 62 - 65

“Trial feasibility was defined as the successful recruitment and retention of trial participants, adherence to the intervention, identification of barriers to the intervention, and the rigorous collection of outcome data.”

2. More details are needed in regards to assessing patient eligibility/ inclusion / exclusion criteria. Were these decisions made from objective measures or subjective choice?

Author's Response:

A study by Schweickert et al is used to support the inclusion criteria. The following text has been added to the Participant section of the Methods as advised.

Line 164 - 165

“Schweickert et al had reported improved functional outcomes in patients who had received physical therapy within 72 hours of the initiation of mechanical ventilation. Thus …”

We used subjective assessments only in reviewing exclusion criteria. The benefit of an objective assessment tool has been acknowledged in the discussion section:

Line 464 - 465

“The exclusion criteria relied on subjective assessments only. Examination of functionality using a validated tool would have strengthened objective assessment.”

3. More clarity is needed regarding the time frame of recruitment, were research staff in the hospital ready to enrol patients over the entire study time frame? every morning?

Author's response: The following text regarding enrolment of participants has been added to the Methods - Participant section.

Line 174 - 176

“During the week, potential participants were identified during the 8am ward round by a member of the research nursing team. Senior medical or nursing staff contacted the on-call member of the research team on the week-end if a suitable participant was identified”
4. Insufficient details are given on obtaining informed consent. Were only patients that were capable of giving informed consent or was consent obtained after randomization when the patients were capable?

Author's response:

Further text regarding consent processes is included in the Methods - Participant section.

Line 177 - 179

“Consent was initially provided by the substitute decision maker as the participant lacked capacity related to altered consciousness, sedation and medical condition. Once able, the participant was asked to provide deferred consent to continue in the study.”

5. Was contamination a problem, whereby staff were potentially administering intervention and control conditions to staff? were other study designs considered to reduce this?

Author's response: The following text regarding the minimization of contamination of the care of the control group is included in the Discussion section.

Line 512 - 522

“Potential contamination of the care of the control group was considered. The intervention group received the standardised and protocolised ABCDE bundle via a prescription within the clinical information system which once ordered could not be ignored or deleted resulting in the delivery of consistent and standard care every day. To provide additional control in our pilot study, only the intervention group had access to the ABCDE protocols via the clinical information system. The protocols were not available in any other format. Alternatively, the control group received care dependent on the medical officers, physiotherapists, occupational therapist, nursing decisions made daily with no use of protocol.” Variation in the control group occurred related to different clinical practice and effort of individuals.

6. Table 1 baseline characteristics contains information regarding length of stay and other patient outcomes (e.g. mortality).

On a side point, was the mortality numbers listed all in-hospital mortality or post discharge as well?

Author's response: The following additional detail regarding mortality data has been added to the Results section.

Line 349 - 350
“Mortality data was collected to the 90-day follow-up. However, all mortality occurred prior to hospital discharge.”