Author’s response to reviews

Title: Pediatric Intensive Care Stress Ulcer Prevention (PIC-UP): A protocol for a pilot randomized trial

Authors:

Mark Duffett (duffetmc@mcmaster.ca)
Karen Choong (choongk@mcmaster.ca)
Jennifer Foster (Jennifer.Foster@iwk.nshealth.ca)
Elaine Gilfoyle (elaine.gilfoyle@ahs.ca)
Jacques Lacroix (j_lacroix@videotron.ca)
Nikhil Pai (pain@mcmaster.ca)
Lehana Thabane (thabanl@mcmaster.ca)
Deborah Cook (debcook@mcmaster.ca)

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Reviewer #1: Well written manuscript outlining a carefully constructed pilot study by a team with extensive experience in clinical trials including in critically ill children. I have only a few minor comments:

1. Why is the inclusion limited to >12 months? While I assume this relates to the baseline bleeding risk - perhaps this should be made clear and referenced. If this is not well evidenced then suggest reconsidering this very significant proportion ~50% of critically ill children as this will limit both the feasibility of the study and the potential impact of the findings. Note that the cited reference from Brazil has not limited to >12 months and hence there is apparently an unanswered question on the utility of acid suppression in this population.

We agree entirely that a lower minimum age is more appropriate and we do not yet have sufficient data on the epidemiology of bleeding in pediatric critical care to support such a minimum age. We had originally planned to include infants less than 1 year of age as well, but Health Canada did not approve enrolling this age group, citing a paucity of safety data. This will reduce the number of eligible patients and limit the generalizability of the results, as infants are a substantial proportion out population of interest. To avoid delay, we started the trial using 1 year
as the minimum age and will re-apply to include infants. We have added this explanation after
the inclusion criteria.

2. RR is introduced without spelling out in full (paragraph 2)

Thanks for catching this.

3. What is the time window for consent? I couldn't see this specifically mentioned.

Although we are attempting to enroll as early in the PICU stay as possible, we don’t have a
specific time window for consent. Page 8 includes “Children may be enrolled in this trial at any
point in their PICU stay once they fulfill the eligibility criteria and have none of the exclusion
criteria for the first time.”

4. Consent rate for placebo drug trials is often lower than for other interventions = 80% sounds
ambitious to me - but will clearly be determined by the pilot."

Despite our best efforts, it may indeed be lower, but this is not one of our feasibility objectives.
We have added “We will monitor the consent rate and solicit feedback from parents to better
understand the modifiable reasons for consent refusal and develop strategies to address these.” to
the section on consent.

5. Participants will be randomized to intravenous pantoprazole or matching placebo once
daily.”

Suggest better as “Participants will be randomized to receive intravenous pantoprazole or
matching placebo once daily.” Otherwise suggests they are randomised each day!

Thanks. We have changed this.

6. The sample size doesn't appear until page 12 - I think this should be in the page 7 study
population also.

Thanks. We have moved it to follow the study population section.
7. 2 or more cases per month is a very low target given the inclusion criteria - but again will be confirmed in the pilot.

We have based this number on our previous trial and our ongoing observational study. The pilot will indeed let us make more accurate estimates for the larger trial.

8. I did not see a planned duration of the trial.

We have added to the sample size section: “We anticipate enrolling over a total of 18 months, with sites starting sequentially over a 6-month period.”