Author’s response to reviews

Title: Acute severe paediatric asthma: study protocol for the development of a core outcome set, a Pediatric Emergency Networks (PERN) study

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** Please note that this response is also contained as a new attachment to the resubmission **

30th September 2019.

Dear Dr Cavalcanti

Re: TRLS-D-19-00698
Acute severe paediatric asthma: study protocol for the development of a core outcome set, a Pediatric Emergency Networks (PERN) study

Thank you for considering our paper, and for the opportunity to respond to the reviewers’ comments. They are reproduced below, along with our responses (in bold).

We look forwards to hearing the outcome of our submission of a revised manuscript.

Yours sincerely,

Prof Simon Craig
On behalf of the authors

Reviewer #1: This is an ambitious project with a great deal of international support. I also think the
goals of the project have wide applicability across the globe. The methodology outlined seems comprehensive and appropriate for the aims. I only have 2 comments for consideration:

1. The goal of step 4 (chart review) is to identify the prevalence of certain outcomes for use in powering future trials. I am unclear as to why the data abstraction is limited to Australia and New Zealand. It is not unreasonable to assume that many of these outcome measures will vary significantly across the globe. Since you have access to the entire PERN network, why limit the data collection to just 2 countries (which will likely yield very similar results)?

The chart review is expected to provide useful information regarding the prevalence of particular outcomes in children with asthma, including pneumothorax, use of non-invasive ventilation, ICU admission, and intubation.

We acknowledge that restricting our chart review to two countries is a potential criticism, however, the decision was made for pragmatic reasons, including: (1) similar work has already been done in the UK and Ireland (and is underway in the USA), (2) the relatively rare incidence of parenteral therapy for asthma (approximately 3% in the UK and Ireland study) would require the review of a large number of charts to identify those receiving such therapy, and (3) funding and time constraints made data collection within the one research network more feasible.

We expect to demonstrate some variation in treatment and outcomes - the PERUKI study (Morris et al, 2015; reference 11 in our manuscript) found that the use of IV therapy varied between hospitals from 0% to nearly 20%.

When considering the work as a whole, we are including many countries when seeking input into relevant outcome measures, and feel that obtaining international consensus on what to measure is the most important aspect of this work. If particular outcomes are identified which need further information, a more targeted international chart review could then be undertaken if needed.

2. I don't have a lot of experience with Delphi procedures, but I would be a little concerned about the consensus definition. It seems like it would be not unlikely for a measure that is extremely important clinically (ie clinical asthma score) to be removed because it didn't show value to the families. Is it typical to essentially allow "veto power" by both groups? I understand that definition 2 essentially allows one group to over-rule the other if they reach 90% consensus, but that is a pretty high bar. If this methodology has proven successful in the past then it should probably remain as is.

We based our consensus definitions on the COMET Handbook (Williamson et al, 2017 – reference 46 in our paper).

Items will be included in the third round if they are rated 7 to 9 (on the 9-point Likert scale) by 50% or more participants and 1 to 3 by no more than 15% of participants in at least one stakeholder group. Consensus is defined as (1) 70% of participants scoring outcomes as 7 to 9 and 15% or less scoring 1 to 3 by both stakeholder groups; or (2) 90% or more scoring 7 to 9 from either stakeholder group. Neither of these definitions allow for a right of “veto” or removal of an outcome by a single stakeholder group.

Reviewer #2: This is a well written and comprehensive study protocol. I congratulate the authors on undertaking this project that is essential and timely.

I have minor comments:

- The study could benefit from the inclusion of allergists and pediatric pulmonologists interviews. The interview study does aim to include a wide variety of participants. We have not been prescriptive with our description of who would be appropriate to include, as the specialty teams involved in the management of acute asthma may vary according to the hospital type and geographic region.
Table 1 provides a description of possible participants: “Group members will also be asked to approach a local colleague from another medical discipline (e.g. emergency physician, paediatrician, intensivist or respiratory paediatrician) to seek their participation.” The term “respiratory paediatrician” is equivalent to the term “pediatric pulmonologist”. Allergists are not specifically mentioned, nor are they specifically excluded from the study.

- The authors could improve their perspectives by systematically reviewing all trials of acute asthma in children and not only those with IV bronchodilators as an outcome as this type of treatment is only occasionally used in general. For example, admission rate in a very important clinical outcome of acute asthma studies that was not mentioned. We accept this criticism, however, in addition to our systematic review on children having IV bronchodilator therapy, we are also conducting an Overview of Cochrane reviews for interventions for escalation of therapy for acute exacerbations of asthma in children (the review protocol is reference 48). This will provide a more comprehensive understanding of currently utilised outcomes for a variety of interventions.

In our systematic review of IV bronchodilator use (the full paper is available as reference 47), admission rate was a primary outcome in one study, and a secondary outcome in two studies. As the paragraph only provided a brief summary of our findings, highlighting the most common outcomes, admission rate was therefore not mentioned.