Reviewer’s report

Title: Fluid strategies and outcomes in patients with acute respiratory distress syndrome, systemic inflammatory response syndrome and sepsis: a protocol for a systematic review and meta-analysis

Version: 0 Date: 10 Sep 2015

Reviewer: Lise Estcourt

Reviewer's report:

This is a protocol for a review on "Fluid strategies and outcomes in patients with acute respiratory distress syndrome, systemic inflammatory response syndrome and sepsis"

This review is likely to be of interest to intensivists.

However there are some amendments required to the protocol. Major amendments include:

Background

1. There are a variety of definitions for sepsis, infection associated with organ failure is only one of the definitions. The authors should highlight this fact and also state they are using the definition that includes associated organ failure for this systematic review.

2. How will it be identified by the authors that the initial fluid resuscitation phase has been excluded from the studies. What definition will be used to define this?

Outcomes

3. What does mortality (as defined by the authors) mean? Do the review authors mean all-cause mortality (time-scales as defined as the studies)? If so any analysis should be clustered over short medium or long time scales. If the authors mean different types of mortality then these should not be combined.

4. If the review is assessing respiratory dysfunction, is it not number of days on a ventilator rather than ventilator-free days?

Study selection

5. Please state why 1980 has been chosen as a cut-off point was there any significant change in management of patients at this time point? Please state why this time has been chosen

Analysis
6. A cluster RCT could be used for studies that try to answer this review's questions, therefore the authors need to pre-specify how they would take account of cluster RCTs in the analysis.

7. Time to event data should preferably be analysed as hazard ratios if data are available. Please add this to the analysis plan as the authors plan to extract mortality data.

8. State how the review would deal with an outcome with rare events (e.g. using Peto).

9. Quality of included studies. The authors have not included an assessment of overall quality of the data but only included an assessment of risk of bias of RCTs. Overall quality assessment for pre-specified outcomes should be performed using a GRADE assessment to highlight the quality of evidence for each outcome. Quality of evidence may differ from outcome to outcome. For example, all-cause mortality is not at risk of bias if the study is unblinded, whereas mortality due to a specific type of mortality may be at risk of bias if the study is unblinded. Please amend.

10. "If two or more studies are available for an outcome, their results will be combined in a meta-analysis". Please clarify that this should only be done if it is appropriate to do so. It may not be appropriate even if there is no statistical heterogeneity if there is clinical heterogeneity or the outcomes are not similar enough (different types of mortality, or mortality over different time scales).

11. Please state how the data would be presented if a meta-analysis could not be performed.

12. Please give examples of sensitivity analyses that will be performed if possible for example only including studies at low risk of bias.

13. For subgroups that have been pre-specified they should be performed if data are available.

Minor amendments

1. Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol.

Level of interest
Please indicate how interesting you found the manuscript:

An article of importance in its field

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable
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