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: 17 Sep 2015

Reviewer: Bram Rochwerg

Reviewer's report:

Thanks for the opportunity to review this protocol. I think the proposed research is important and will be informative to practicing clinicians and those designing future clinical trials.

Although the protocol is well done I have a few suggestions/points to consider prior to publication:

1) study inclusion - the authors state that studies including perioperative patients or heart failure patients will be excluded. Will studies with mixed patient populations (ie 20% CHF patients) be included?

2) Outcomes - Any minimal duration or maximal duration for followup for the primary outcome? What if a study reports multiple time points for mortality outcome data?

   AKI obviously has many different definitions - how will this be handled?

3) ROB Assessment - I believe there is an accidental omission as right now this section states that domains will be rated as either low or unclear risk of bias with no mention of an option for 'high'.

   - the Ottawa Newcastle scale has a slightly different version for cohort studies or case-controlled studies

   - only the cohort version is shown

   - I believe case-controlled studies would be included in this review?

4) Statistical Heterogeneity - the authors state that if high (>90%) then results will be presented narratively - what if heterogeneity is high but can be explained by a priori subgroup analysis? Then will they still not show the quantitative analysis? I would think it would be useful in this case. Potential revision would be if significant 'unexplained' statistical heterogeneity.
5) Analysis Plan - This section requires a little clarification. Do the authors plan to present all outcome data across clinical syndromes (ARDS, SIRS, sepsis)? If this is the case then I'm not 100% convinced how this will enhance generalizability of the results compared to looking at all critically ill patients (including those that don't meet one of the clinical syndromes mentioned). If the plan is to present all outcome data separately then subgroups will be shown within ARDS? eg ARDS children/ARDS adults?

- What factors will be considered to determine suitability of data for subgroup testing? when specifying subgroups a priori it is suggested to hypothesize direction of subgroup effect which will lend to increasing credibility

- how will you handle outcomes that have both observational and RCT data? Will both be shown?

- for observational data, the authors have mentioned that previous criticisms of primary publications have stated that sicker patients will usually get more fluid which may bias results - will you use raw data or adjusted data (for other prognostic factors, if available) for observational studies?

6) Certainty in Evidence assessment - do the authors plan for any assessment of the evidence across outcomes? eg GRADE as per point 17 of the PRISMA-P guidelines

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