Author’s response to reviews

Title: Prevalence and prognosis of acutely ill patients with organ failure at arrival to hospital: Protocol for a systematic review

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Author’s response to reviews:

Dear editor

We thank you for considering the manuscript in a revised form.

We would like to thank you and the reviewers for your constructive criticism and ideas for improvements. We believe the new version is improved.

We confirm that all author details are correct, and all authors have read and approved the revised manuscript.

Yours sincerely

Peter Bank Pedersen, MD
Reviewer reports:

Reviewer #1: This manuscript is a protocol describing an approach to systematically reviewing the literature to ascertain the prevalence and prognosis of acutely ill patients with organ failure who present to hospital. This is an important topic and a systematic review in this area will be helpful for readers. There are some methodological points that should be clarified to strengthen this protocol:

Major Concerns:

1. Is a second information scientist going to peer review the search strategy (e.g. using the PRESS checklist)?

Answer: A relevant point addressed by the reviewer. We were not aware of the PRESS checklist when the search strategy was developed, and only help from one information specialist was planned.

Changes to manuscript: Search strategy paragraph: Search strategy for the databases, will be developed iteratively by input from all members of the project team, and with help form an information specialist from The Medical Research Library at University of Southern Denmark, in a face to face meeting.

2. Are you going to limit your search to a specific time period (e.g. from 1995 onward)?

Answer: The limits are set by the time periods covered by electronic databases used.

Changes to manuscript: Information sources paragraph: Information sources used, are electronic databases, not restricted to a specific period of time, references in included studies and review articles, and authors’ personal files.
3. Are you going to include the grey literature in your search strategy?

Answer: A very relevant question stated by the reviewer. The search strategy does not include grey literature; this will be outlined under the limitations paragraph in the final systematic review.

4. Why is only one author going to conduct screening of titles and abstracts?

Answer: Due to lack of time, we decided to leave out a second author to perform titles and abstracts screening.

5. Are you going to do a calibration exercise prior to full-text screening to ensure good agreement between reviewers?

Answer: Prior to full-text screening, inclusion and exclusion criteria are defined, but no calibration exercise are planned. The proportion of agreement, between the two reviewers performing full-text screening, is presented in the final systematic review.

Changes to manuscript: Selection process paragraph: Other studies will be read in full length, independent and in duplicate, by two review authors, PBP and DLN. Subsequently, in agreement, the two review authors will decide, whether the study meets inclusion criteria. The proportion of agreement is presented in the final review. Disagreements will be discussed, at a face to face meeting, and in case of continued disagreements, AH and ATL’s point of view, will decide inclusion.

6. If there are randomized controlled trials included in your systematic review, what critical appraisal tool will be used?

Answer: The reviewer addresses a very relevant point. Based on scoping searches, we do not expect any randomized controlled trials to fulfil inclusion and exclusion criteria; otherwise the Cochrane Risk of Bias Tool will be used.

Changes to manuscript: Risk of bias in individual studies paragraph: To assess the risk of bias within included studies, the Quality in Prognosis Studies (QUIPS) tool for prognostic studies, the
Newcastle-Ottawa Scale (NOS) for observational studies, and the Cochrane Risk of Bias Tool (CRBT) for randomized controlled trials, will be used. The CRBT rates; selection bias, performance bias, detection bias, attrition bias, reporting bias, and other bias; as low, high, or unclear.

7. Will the final decision to conduct meta-analyses be based on clinical, methodological, or statistical heterogeneity? Or all three sources of heterogeneity?

Answer: The final decision to conduct meta-analyses will be based on all three abovementioned sources.

8. You mention in the abstract that random-effects meta-analyses will be used to pool effect estimates, but this is not stated in the data synthesis section of the manuscript. It will be helpful to further describe the possible methods that you will use to conduct meta-analyses.

Answer: Thanks to the reviewer to point out the absence of description in the data synthesis section.

Changes to manuscript: Data synthesis paragraph: If heterogeneity is low, contrary to expectation, we will present conduct a random effects meta-analysis, stratified by basic study design. We will present both synthetic and analytic views, and try to explain heterogeneity by study characteristics, and population characteristics.

Minor Concerns:

1. The manuscript would be strengthened by having an English copy writer review the manuscript for spelling and grammatical errors.

Answer: The manuscript passes all authors for proofreading before resubmission. This time also for correcting spelling and grammatical errors, some authors are fluent English writers.
2. Consider using the term delirium as opposed to cerebral failure. Readers will likely be more familiar with the term delirium.

Answer: The term cerebral failure was chosen over delirium, as it describes cerebral impact in a wide sense.

3. In the methods section of the abstract, please ensure it is clear that two authors will be conducting full-text article screening.

Answer: We will clarify abovementioned.

Changes to manuscript: Abstract, Methods paragraph: By independent full-text screening, two authors will decide on eligibility for the remaining studies.

4. In the outcomes and prioritization section, consider adding an additional sentence that clarifies how your secondary outcomes will be operationalized (e.g. "If a patient develops organ failure, what is the relative risk of transfer to the ICU and/or 30-day or 1-year all-cause mortality?")

Answer: We will add proposed.

Changes to manuscript: Outcomes and prioritization paragraph: The secondary outcome, for patients with organ failure, is prognosis, as assessed by proportion and relative risk of transfer to ICU and/or 30-day (or as close as possible) and 1-year (or as close as possible) all-cause mortality.