Reviewer's report

Title: Protocol for a Systematic Review and Individual Patient Meta-Analysis of Benefit of So-Called Lung-Protective Ventilation-Settings in Patients Under General Anesthesia for Surgery

Version: 1 Date: 14 October 2013

Reviewer: Dean Langan

Reviewer's report:

Overall, this was a well-written protocol that for the most part is clear and reproducible. The background section shows that this is important research and highlights a clear gap in current evidence base.

Major Compulsory Revisions

1. Background

The protocol makes clear why there is a need for this IPD research to be conducted, given that there is insufficient power from existing meta-analyses. However, I feel there should be a little more information on the existing meta-analyses included in the background section. I assume that the existing meta-analyses are not IPD, but this is not stated. Also, the background section suggests that there are 4 distinct pieces of evidence: two meta-analyses and two RCTs. What studies were included in these meta-analyses? Was there an overlap in the studies included in the meta-analyses and were the RCTs mentioned included in any of the meta-analyses? Finally, when were the meta-analyses conducted and is this meta-analysis likely to find new evidence?

2. Methods: Search strategy

Will studies that have already been mentioned in the background section be included in this meta-analysis? This includes studies found within the meta-analyses.

3. Analysis plan

Outcome 4 is length of stay in hospital, defined as the time from hospital admission to hospital discharge. How will in-hospital mortality be treated for this outcome?

4. Methods: Completeness of data

The middle of surgery time-period is defined as “total time of procedure divided by two”. It’s unlikely that data will contain measures exactly in the middle of surgery. More details needed as to how data will be used for this time-period.

5 Methods: Statistical analysis
Which will be the primary analysis out of ITT and per protocol?

Why is tidal volume coded differently for ITT and per protocol?

Statistical methods need to be defined for all types of outcome, not just time to event. Statistical methods are clear for the restricted cubic splines analysis and cox proportional hazards model but not for binary outcomes.

For the generalised linear model used on time-course variables, it states “The model includes two factors: 1) study group (fixed factor)…” What is meant by study group?

Minor Essential Revisions

1. General

No information is contained in the protocol about dissemination of the results.

2. Methods: Search strategy

At the end of the section on “search strategy”, there is information on how authors will be contacted and how data will be extracted from each studies database. This would be more appropriate in the section titled “collection of individual patient data”.

3. Methods: Collection of individual patient data

The section on “search strategy” suggests that databases will be sent to the corresponding author for data extraction which is inconsistent with the section “collection of individual patient data”. This section states that a datasheet will be sent to authors. More clarity on data collection is needed.

4. Methods: Completeness of data

My clinical knowledge is limited, so correct me if I’m wrong. Are all surgeries going to be at least, say, 3 hours long? Beginning of surgery measures are in the first hour and end of surgery measures are in the last hour, so I assume one hour is only a small amount of time relative to the duration of the surgery in all cases?

5. Model

I would recommend changing the title of this section to “model selection” and adding anything that does relate to model selection into the “statistical analysis” section.

6. Discussion

There is repetition of results from the existing meta-analyses and clinical trials in the discussion section; these were already mentioned in the background.

The discussion states “The use of low tidal volume can increase the use of sedatives and muscle relaxants increasing the incidence of ICU delirium and ICU
acquired weakness”. It could be interesting to investigate whether sedatives and muscle relaxants are a mediator variable for the primary outcomes.

Discretionary Revisions

1. Methods: Completeness of data

For the middle of surgery time period, it states “middle of the surgery, beginning of the surgery, defined as the parameters…”. Is “beginning of the surgery” a typo – this doesn’t make sense?

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests