

ADDENDUM

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This is an addendum to the protocol titled "*Apparently conclusive meta-analyses may be inconclusive - The reliability of positive, neutral, and negative results in apparently conclusive critical care meta-analyses. Authors: F Keus, G Imberger, J Wetterslev, C Gluud, SL Klingenberg, JG Zijlstra, ICC van der Horst. Version: 05-04-2013.*", which was published on the Copenhagen Trial Unit (CTU) homepage website (www.ctu.dk).

The motivation for this addendum to the previous protocol is based on recent advancements in the evaluation of the risks of bias of systematic reviews. For transparent reporting of systematic reviews the PRISMA statement has been introduced and although some domains of bias risk are included in this tool for reporting evaluation, it is not a strict bias risk assessment tool.¹ Only recently, however, the ROBIS tool has emerged for assessment of the risk of bias of systematic reviews.²

There are three very basic domains of potential risk of bias which should be assessed as low risk before any review/meta-analysis can be considered sufficient scientifically rigorous and to be qualified systematic.^{2,3}

In adherence to our previous protocol we will assess the concerns of any potential risks of bias of all selected meta-analyses identified by our search strategy according to the following domains:

1. The reference to and public availability of **any prepublished protocol** prior to the conduct of the (systematic) review and/or meta-analysis.
2. The reference to and availability of a **full search string exploring more than two databases** either available in the full manuscript, or as additional material or published in the referenced protocol.
3. The reporting of the use of **any evaluation of the risk of bias** and the results originating from these assessments of the included trials/studies, independent the tool or method used to evaluate bias risk.

The selected meta-analyses assessed as low risk on all these three domains of potential risks of bias of systematic reviews will be subjected to a full ROBIS and PRISMA evaluation.

We will report our results using a flow diagram illustrating the numbers of meta-analyses after each step of these three basic bias risk domains assessments.

References

1. Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PLoS Med* 6(7).
2. Whiting P, Savović J, Higgins JP, Caldwell DM, Reeves BC, Shea B, Davies P, Kleijnen J, Churchill R; ROBIS group. ROBIS: A new tool to assess risk of bias in systematic reviews was developed. *J Clin Epidemiol.* 2016 Jan;69:225-34.
3. Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. *The Cochrane Collaboration, 2011.* Available from www.handbook.cochrane.org.