Author's response to reviews

Title: The aprotinin saga and the risks of conducting meta-analyses on small randomised controlled trials - a re-analysis of a Cochrane report

Authors:

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Comments to the reviewers:

Reviewer 1:

The reviewer disagrees on my conclusions which he is fully entitled to. However, I believe we both agree that placebo controlled randomized double blind studies are still the gold standard if they are properly conducted and have statistical power. My main message was to stress that studies which do not have focus on the main outcome (mortality in this case) and have other methodological flaws are not reliable even if they are RCTs.

Reviewer 2:

1. I have changed the title according to the reviewer’s suggestion
2. I have included confidence intervals in the BART and the observational studies.
3. Revised according to the reviewer’s suggestion.
4. Included a comment that the editorial appeared before publication of the BART study.
5. Aprotinin was withdrawn by the company. This is now included in the text.
6. A forest plot did not show any clear pattern even if three out of the four largest studies showed point estimates above 1. However, I would prefer to interpret this cautiously without any comments.
7. and
8. The reviewer makes some interesting points concerning the observational study by Dietrich (1992). I have therefore includes the following sentences: “This study was conducted before the FDA approval in 1993 when there was no suspicion of adverse effects. This is apparent from the study design with no focus on mortality and no control for confounding factors”
I enclose one version with corrections marked and one without.

Måns Rosén