Reviewer's report

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

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Reviewer: Jerrold Levy

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The authors suggest the aim of their paper is to review the quality of the meta-analysis of a Cochrane report. Although the authors suggest none of the RCTs had sufficient statistical power to detect differences in mortality, the purpose of Meta analyses is to take high quality data and pool it. The authors suggest it is doubtful whether small studies should be included in meta-analyses if they do not have the purpose of studying the specified outcome and if the follow-up method or time is not adequately described. The aprotinin saga shows overconfidence in small RCTs of inferior quality compared to well-conducted observational studies.

This reviewer disagrees- observational studies all have problems with decisions on use of a drug based on factors that usually include different risks, i.e., sicker patients get different therapies. What the authors suggest is contrary to current thinking, although with propensity and other analyses, the data sets can be better balanced. Nonetheless, placebo controlled randomized double blind studies are still the gold standard.