**Meta-analysis – the case *for***

**Rebuttal**

David W. Mudge[1], Angela C. Webster[2], and David W. Johnson[1]

Author affiliations:

1. The University of Queensland at Princess Alexandra Hospital, Brisbane, Australia
2. The University of Sydney, Sydney, Australia

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**Corresponding author**

A/Professor David W. Mudge

Department of Nephrology,

Level 2, ARTS Building,

Princess Alexandra Hospital

Ipswich Road

Woolloongabba

Queensland

Australia 4102

email: david.mudge@health.qld.gov.au

tel: +61 7 3176 5080

fax: +61 7 3176 5480

Firstly, we would like to acknowledge that our opponents have conceded that meta-analysis is very useful and is increasingly being used to aid clinical decision making, including by nephrologists. They also agree with a key message of our original argument that clinicians and policy makers must carefully and critically appraise all research studies, including meta-analyses, before changing practice.

However, we strongly refute our opponents' argument that "an effect unable to be ascertained unless trial results are pooled together is not an important effect." Specifically, we previously reported several examples from the nephrology literature whereby meta-analysis revealed important practice-changing benefits or harms that were not apparent in most or all of the original randomised trials. These included the mortality benefit of CMV prophylaxis in kidney transplantation and the reduction in proteinuria progression with renin-angiotensin blockers in diabetic kidney disease progression.

Our opponents also discussed the impact of heterogeneity, citing the example of N-acetylcysteine administration for prevention of contrast nephropathy, to illustrate their point that differing effect sizes might have been the explanation. Although there are very limited trial data with adequate reporting of hard clinical endpoints to support the use of this intervention, we should nevertheless again emphasise that meta-analysis allows authors to identify trial heterogeneity and to tease out factors contributing to it through sub-group or meta-regression analyses. For example, in a meta-analysis of cyclosporin versus tacrolimus for kidney transplant immune suppression, although tacrolimus was found to be superior for preventing renal allograft rejection at one year, clinical heterogeneity was also identified insofar as higher tacrolimus doses diminished this benefit and resulted in a

higher incidence of post-transplant diabetes mellitus[1]. Furthermore, heterogeneity related to trial design and bias risk is likely to be less of an issue in the future, given that randomised controlled trial registration and reporting has significantly improved[2], as has their quality following journal adoption of the CONSORT checklist[3]. This should in turn enhance the clinical impact of meta-analyses.

Finally, with respect to the influence of poor quality studies, we would like to reiterate the point that an objective bias risk assessment of included studies should form part of all systematic reviews and meta-analyses, and that the potential impact of poor quality studies on the conclusions of a meta-analysis can be examined through sensitivity analyses that exclude such studies.

**References**


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