Meta-analyses of Clinical Drug Trials—Gold Standard Reviews or Statistical Alchemy?

E S Y Chan,* BSc, BVMS, PhD

Abstract

Renewed emphasis on the critical appraisal of published evidence has in turn led to critical appraisal of the way clinical studies have been reviewed. Reviews perform the vital function of summarising a wealth of research information in an efficient and trustworthy manner, but traditional narrative reviews have fallen short in this area, not because they are narrative, but because they have allowed reviewer and publication bias to creep in under the guise of expert authority. Meta-analysis or systematic review emphasises the use of a review protocol based on logical principles to minimise bias, together with qualitative and appropriate quantitative summaries of the data. Like any review, the perceived impact of a meta-analysis is dependent on the quality of the reviewed studies, therefore randomised clinical trials are the favoured substrate for the meta-analysis of drug efficacy because of their potentially high internal validity. The importance of meta-analysis as a tool for clinical drug evaluation has prompted this selective account of its nature, theory, practice and interpretation, with particular emphasis on meta-analysis as a review methodology rather than a statistical methodology, the critical distinction between design and result homogeneity and the need to explore issues of heterogeneity rather than gloss over them by using some statistical shortcut.

Key words: Exchangeability, Fixed-effects model, Heterogeneity, Homogeneity, Individual patient data meta-analysis, Nested meta-analysis, Random-effects model, Study precision, Systematic reviews, Weighted average

* Head and Co-ordinator
Division of Evidence-based Medicine
NMRC Clinical Trials and Epidemiology Research Unit, Ministry of Health, Singapore
Address for Reprints: Dr Edwin Chan Shih-Yen, Clinical Trials and Epidemiology Research Unit, 10 College Road, Singapore 169851.
E-mail: edwin@cteru.gov.sg