

Education and debate

Systematic Reviews: Rationale for systematic reviews

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Systematic literature reviews including meta-analyses are invaluable scientific activities. The rationale for such reviews is well established. Health care providers, researchers, and policy makers are inundated with unmanageable amounts of information; they need systematic reviews to efficiently integrate existing information and provide data for rational decision making. Systematic reviews establish whether scientific findings are consistent and can be generalised across populations, settings, and treatment variations, or whether findings vary significantly by particular subsets. Meta-analyses in particular can increase power and precision of estimates of treatment effects and exposure risks. Finally explicit methods used in systematic reviews limit bias and, hopefully, will improve reliability and accuracy of conclusions.

Systematic literature review is a fundamental scientific activity. Its rationale is grounded firmly in several premises. Firstly, large quantities of information must be reduced into palatable pieces for digestion. Over two million articles are published annually in the biomedical literature in over 20 000 journals¹ - literally a small mountain of information. For example, about 4400 pages were devoted to approximately 1100 articles in the BMJ and New England Journal of Medicine, combined, in 1992. In a stack, two million such articles would rise 500 m. Clearly, systematic literature review is needed to refine these unmanageable amounts of information. Through critical exploration, evaluation, and synthesis the systematic review separates the insignificant, unsound, or redundant deadwood in the medical literature from the salient and critical studies that are worthy of reflection.²

Secondly, various decision makers need to integrate the critical pieces of available biomedical information. Systematic reviews are used by more specialised integrators, such as economic and decision analysts, to estimate the variables and outcomes that are included in their evaluations. Both systematic and more specialised integrations are used by clinicians to keep abreast of the primary literature in a given field as well as to remain literate in broader aspects of medicine.^{3,4} Researchers use the review to identify, justify, and refine hypotheses; recognise and avoid pitfalls of previous work; estimate sample sizes; and delineate important ancillary or adverse effects and covariates that warrant consideration in future studies. Finally, health policy makers use systematic reviews to formulate guidelines and legislation concerning the use of certain diagnostic tests and treatment strategies.

An efficient scientific technique

Thirdly, the systematic review is an efficient scientific technique. Although sometimes arduous and time consuming, a review is usually quicker and less costly than embarking on a new study. Just as important, a review can prevent meandering down an already explored path. Continuously updated literature review, as exemplified by the Oxford Database of Perinatal Trials, can shorten the time between medical research discoveries and clinical implementation of effective diagnostic or treatment strategies.⁵ A landmark example of cumulative meta-analyses and its benefits is shown in figure 1, which gives odds ratios and 95% confidence intervals for 33 trials that compared intravenous streptokinase with a placebo or no therapy in patients who had been hospitalised for acute myocardial infarction. The left side of the figure shows that the effect of treatment with streptokinase on mortality was favourable in 25 of the 33 trials, but in only six was statistical significance achieved. The overall pooled estimate of treatment effect given at the bottom significantly favoured treatment. The right side of the figure shows the same data presented as if a new or cumulative meta-analysis was performed each time the results of a new trial were reported. The years during which the treatment effect became statistically significant were 1971 for a two sided P value of <0.05, 1973 for a P value of <0.01, and 1977 for a P value of <0.001. This cumulative type of review indicated that intravenous streptokinase could have been shown to be life saving almost 20 years ago, long before its submission to and approval by the United States Food and Drug Administration and its general adoption in practice.

FIG 2 - The Cochrane Collaboration logo shows how pooling data reveals the significance of treatment effects

FIGURE OMITTED

Eighthly, quantitative systematic reviews allow increased precision in estimates of risk or effect size. On the right side of figure 1 the cumulative meta-analysis shows that increasing sample size from temporally consecutive studies resulted in continued narrowing of confidence intervals even though efficacy had been established in the early 1970s.⁶ Particularly noteworthy, two very large trials - the 1986 study of the Gruppo Italiano per lo Studio della Streptochinasi nell'Infarto Miocardico (GISSI) involving 11 712 subjects and the 1988 second international study of infarct survival (ISIS-2) involving 17 187 subjects - did not change the already established evidence of efficacy, though they increased precision by narrowing the confidence intervals slightly.

Accurate assessment

A final rationale for systematic reviews is accuracy, or at least an improved reflection of reality. Traditional reviews have been criticised as haphazard and biased, subject to the idiosyncratic impressions of the individual reviewer.¹¹ Systematic reviews and meta-analyses apply explicit scientific principles aimed at reducing random and systematic errors of bias.¹² But whether such reviews will lead to greater reliability, and by inference greater accuracy, is not yet established clearly.⁸

At the very least, the use of explicit methods allows assessment of what was done and thus increases the ability to replicate results or understanding of why results and conclusions of some reviews differ. In addition, reviewers using traditional methods are less likely to detect small but significant effects than are reviewers using formal systematic and statistical techniques.¹³ Finally, traditional review recommendations lag behind and sometimes vary significantly from continuously updated or cumulative meta-analyses.¹⁴ Figure 3 shows that pooled data from 15 randomised trials published before 1990 found no mortality benefit associated with prophylactic lidocaine for acute myocardial infarction. Despite this evidence, most pertinent traditional reviews continued to recommend prophylactic lidocaine. Antman et al have shown also that many effective treatments for reducing mortality due to acute myocardial infarction, such as intravenous magnesium, are not being recommended as often as they might be.^{6,14}

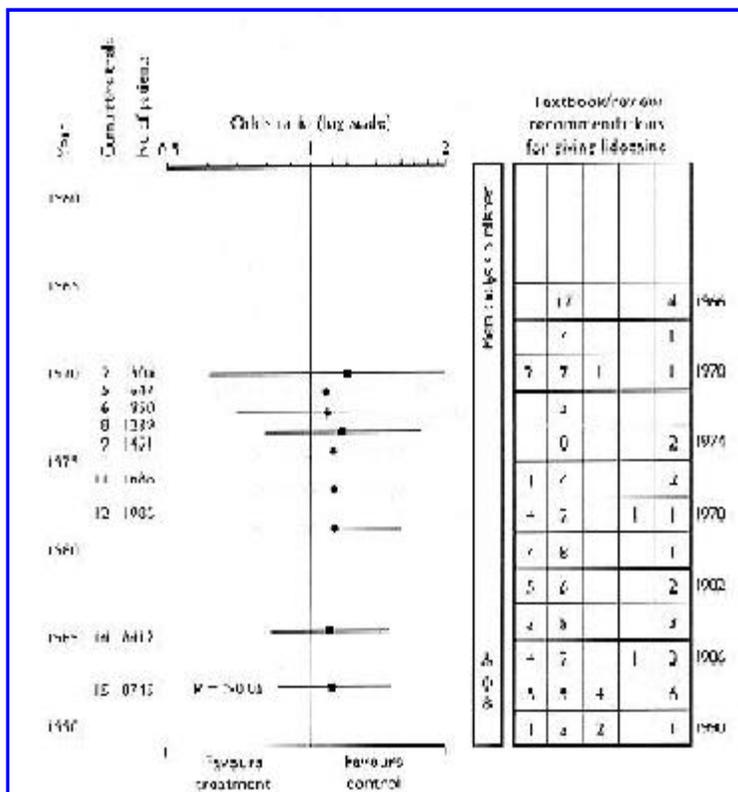


FIG 3 - Cumulative meta-analysis by year of publication or randomised controlled trials of prophylactic lidocaine for acute myocardial infarction, and recommendations of clinical expert reviewers (adapted from Antman et al¹⁴)

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There are a myriad of reasons to herald systematic literature reviews including meta-analyses. The hundreds of hours spent conducting a scientific study ultimately contribute only a piece of an enormous puzzle. The value of any single study is derived from how it fits with and expands previous work, as well as from the study's intrinsic properties.¹⁵ Through systematic review the puzzle's intricacies may be disentangled.

The vast amount of available information under-scores the value of systematic reviews. As T S Eliot asked in his poem "The Rock," "Where is the knowledge we have lost in information?" Moreover, decision makers of various types are inundated with unmanageable amounts of information. They have great need for systematic reviews that separate the known from the unknown and that save them from the position of knowing less than has been proved.¹⁶

Advantages of the systematic review are many. Whether scientific findings are consistent and can be generalised across populations, settings, and treatment variations or whether findings vary significantly by particular subsets can be gleaned. Unique advantages of quantitative systematic reviews or meta-analyses are increased power and precision in estimating effects and risks. Hopefully, both qualitative and quantitative systematic reviews, with their explicit methods, will limit bias and improve the reliability and accuracy of recommendations.

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1. Ad Hoc Working Group for Critical Appraisal of the Medical Literature. Academia and clinic: a proposal for more informative abstracts of clinical articles. *Ann Intern Med* 1987;106:598-604.
2. Morgan PP. Review articles. 2. The literature jungle. *Can Med Assoc J* 1986;134:98-9.
3. Garfield E. Reviewing review literature. Part 2. The place of reviews in the scientific literature. *Current Contents* 1987;30:3-5.
4. Lederberg J. Introduction. *Annual Review of Computer Science* 1986;1:5-9.
5. Chalmers I, Hetherington J, Newdick M, Mutch L, Adrian G, Enkin M, et al. The Oxford Database of Perinatal Trials: developing a register of published reports of controlled trials. *Controlled Clin Trials* 1986;7:306-24.
6. Lau J, Antman EM, Jimenez-Silva J, Kupelnick B, Mosteller F, Chalmers TC. Cumulative meta-analysis of therapeutic trials for myocardial infarction. *N Engl J Med* 1992;327:248-54.
7. Light RJ, Pillemer DB. Summing up: the science of reviewing research. Cambridge: MA: Harvard University Press, 1984.
8. Dickersin K, Berlin JA. Meta-analysis: state-of-the-science. *Epidemiol Rev* 1992;14:154-76.
9. Bossel JP, Blanchard J, Panak E, Peyrioux JC, Sacks H. Considerations for the meta-analysis of randomized clinical trials. *Controlled Clin Trials* 1989;10:254-81.
10. Gelber RD, Goldhirsch A. Meta-analysis: the fashion of summing-up evidence. *Ann Oncol* 1991;2:461-8.
11. Mulrow CD. The medical review article: state of the science. *Ann Intern Med* 1987;106:485-8.
12. Oxman AD, Guyatt GH. Guidelines for reading literature reviews. *Can Med Assoc J* 1988;138:697-703.
13. Cooper HM, Rosenthal R. Statistical versus traditional procedures for summarizing research findings. *Psychol Bull* 1980;87:442-9.
14. Antman EM, Lau J, Kupelnick B, Mosteller F, Chalmers TC. A comparison of results of meta-analyses of randomized control trials and recommendations of clinical experts. *JAMA* 1992;268:240-8.
15. Cooper HM. The integrative research review: a systematic approach. Beverley Hills, CA: Sage Publications, 1984.
16. Glass GV. Primary, secondary, and meta-analysis of research. *Educational Researcher* 1976;5:3-8.

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- Olsen, O., Middleton, P., Ezzo, J., Gotzsche, P. C, Hadhazy, V., Herxheimer, A., Kleijnen, J., McIntosh, H. (2001). Quality of Cochrane reviews: assessment of sample from 1998. *BMJ* 323: 829-832
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- Ernst, E., Pittler, M. H (2001). Assessment of therapeutic safety in systematic reviews: literature review. *BMJ* 323: 546-546 [\[Full text\]](#)
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- Burke, D., BMed, (2000). Review: studies of different interventions have mixed results for psychosocial outcomes after stroke. *Evid Based Ment Health* 3: 80-80 [\[Full text\]](#)
- Campbell, M. K., Daly, C., Wallace, S. A., Cody, D. J., Donaldson, C., Grant, A. M., Khan, I. H., Lawrence, P., Vale, L., MacLeod, A. M. (2000). Evidence-based medicine in nephrology: identifying and critically appraising the literature. *Nephrol Dial Transplant* 15: 1950-1955
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- Tasche, M J A, Uijen, J H J M, Bernsen, R M D, de Jongste, J C, van der Wouden, J C (2000). Inhaled disodium cromoglycate (DSCG) as maintenance therapy in children with asthma: a systematic review. *Thorax* 55: 913-920 [\[Abstract\]](#) [\[Full text\]](#)
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- Richards, D M, Hill, J, Scott, N A, Bancewicz, J, Irving, M. (1995). Open technique has lower evidence of complications. *BMJ* 311: 1090a-1090 [\[Full text\]](#)
- Stichele, R. H V., Dezeure, E. M, Bogaert, M. G (1995). Systematic review of clinical efficacy of topical treatments for head lice. *BMJ* 311: 604-608 [\[Abstract\]](#) [\[Full text\]](#)

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- Bero, L. A, Grilli, R., Grimshaw, J. M, Harvey, E., Oxman, A. D, Thomson, M. A. (1998). Getting research findings into practice: Closing the gap between research and practice: an overview of systematic reviews of interventions to promote the implementation of research findings. *BMJ* 317: 465-468 [\[Full text\]](#)
- Haines, A., Donald, A. (1998). Getting research findings into practice: Making better use of research findings. *BMJ* 317: 72-75 [\[Full text\]](#)
- (1997). Collaborative systematic review of the randomised trials of organised inpatient (stroke unit) care after stroke. *BMJ* 314: 1151-1151 [\[Abstract\]](#) [\[Full text\]](#)
- Kerridge, I., Lowe, M., Henry, D. (1998). Personal paper: Ethics and evidence based medicine. *BMJ* 316: 1151-1153 [\[Full text\]](#)
- Geddes, J., Reynolds, S., Streiner, D., Szatmari, P. (1997). Evidence based practice in mental health. *BMJ* 315: 1483-1484 [\[Full text\]](#)
- Egger, M., Smith, G. D., Schneider, M., Minder, C. (1997). Bias in meta-analysis detected by a simple, graphical test. *BMJ* 315: 629-634 [\[Abstract\]](#) [\[Full text\]](#)
- Duley, L. (1997). Commentary: Sources of bias must be controlled. *BMJ* 315: 220-220 [\[Full text\]](#)

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