

ABC of Methodology

Starting from this issue of *Epidemiologia e Psichiatria Sociale* a new Section, called ABC of Methodology, will regularly cover methodological aspects related to the design, conduct, reporting and interpretation of clinical and epidemiological studies. We hope that these articles will help develop a more critical attitude towards research findings published in the international literature and, additionally, we wish to help promote the implementation of original research projects with higher standards in terms of design, conduct and reporting.

What is a systematic review?

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Making clinical decisions is a key component of everyday clinical practice. To do that, physicians combine their own clinical expertise and training with high quality scientific evidence (Guyatt et al., 2000). In order to keep abreast of scientific evidence, physicians need reliable systems for summarising primary research findings into a form that provides a trustworthy overview of current evidence. The terms review, systematic review, overview, meta-analysis and pooled-analysis, although often used interchangeably, refer to different ways of summarising primary research findings. This note will highlight the main characteristics of these summaries of the literature, with particular emphasis on techniques that allow to perform statistical re-analyses of the available information.

A first relevant distinction should be made between *narrative* and *systematic reviews* (figure 1). Systematic reviews (sometimes called "overviews") collect all studies that address a clearly defined clinical question. Systematic reviews do not select studies according to implicit parameters but employ explicit methodological strategies to identify and synthesise all studies on a specific topic (Mulrow, 1994). This aspect is crucial to avoid *systematic errors*

(*biases*). Biases are distortions that systematically affect results. Examples of biases include the systematic exclusion of: studies published in languages other than English, studies published many years ago, studies reporting results in contrast with the author's beliefs, unpublished studies, and so on. Clearly, different explicit criteria, leading to different studies included in the analysis, may be employed to address the same clinical question. Consequently, systematic reviews can lead to different and sometimes contrasting results that require careful appraisal and interpretation. As new research evidence is continuously published, high-quality systematic reviews are regularly updated (see Cochrane Handbook for Systematic Reviews free full text at www.cochrane.org/resources/handbook/).

By contrast, narrative reviews (sometimes called *traditional reviews*) do not employ explicit methodological strategies to identify relevant studies, and do not report a section describing the methods used to synthesise results. Implicit criteria are used to select studies. Narrative reviews are mainly based on the experience and subjectivity of the author, who is often an expert in the area. Although narrative reviews can be useful to summarise different aspects of complex questions, it has been shown that the absence of clear and explicit methodological strategies to identify studies increases the possibilities of erroneous interpretations of study findings (<http://www.york.ac.uk/inst/crd/>). Thus, the conclusions of narrative and systematic reviews can differ substantially and dramatically.

It is possible that authors of systematic and narrative reviews extract specific information from the included

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studies (usually outcome data) and re-analyse these data using meta-analytical techniques (Thompson & Higgins, 2005). Re-analyses of primary data provide overall estimates of treatment effect that have greater power and precision than any of the constituent studies. These overall estimates constitute a summary of evidence that takes into account the results of each individual study included in the re-analysis (usually weighted estimates are calculated, with weights based on each study's sample size). As shown in the figure 1, re-analyses of data extracted from studies included in systematic reviews are called meta-analyses, while re-analyses of data extracted from studies included in narrative reviews are called pooled-analyses.¹ It's worth reminding that the term *meta-analysis* was used for the first time in 1977 by Smith and Glass, who carried out a systematic review on the effects of psychotherapy.

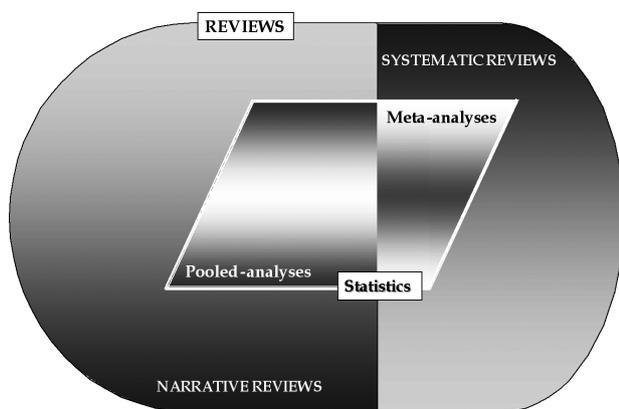


Figure 1. – Graphic representation of the concept of narrative and systematic review, meta-analysis and pooled-analysis

Generally speaking, statistical re-analyses provide misleading results when applied outside the context of a systematic review. In pooled-analyses the inclusion and re-analyses of a selection of all available studies inevitably leads to biased estimates of treatment effect. The systematic exclusion of unpublished studies (usually studies with negative findings), for example, overemphasises the effect of new medicines (Whittington *et al.*, 2004). Additionally, it should be considered that the meta-analytical approach is not an essential part of a systematic review. It may be

¹ The term pooled-analysis is also used to describe re-analyses of individual patient data. Re-analyses of individual patient data will be discussed in one of the next issues of ABC of Methodology.

inappropriate to calculate statistical summaries of individual studies when outcomes are, for example, too different. The inappropriate pooling of data from disparate studies has been exemplified as “combining oranges and apples”, with the likely consequence of reaching meaningless results. However, if studies are not that different, the meta-analytical approach increases the overall sample size and power of the analysis.

The quality of studies included in the systematic review is another relevant factor that should always be considered (Moher *et al.*, 1999). Re-analyses of poor quality data provide poor quality results (“garbage in - garbage out”). It has been shown that many qualitative aspects (allocation concealment, randomisation, blinding, intention-to-treat analysis) have an effect on the direction of treatment results. Studies of poor methodological quality tend to overestimate the effect of the intervention and real differences may be obscured.

When approaching a review article, physicians should initially consider if the review is systematic. If yes, critically appraise the following aspects: (a) authors’ affiliation and financial support (reviews supported by drug companies tend to overemphasise the efficacy of pharmacological treatments); (b) methods employed to identify and select articles; (c) update of the literature search; (d) quality of primary studies; (e) appropriateness of re-analyses; (f) statistical significance, clinical significance and robustness of the results.

Ideally, clinicians should integrate the results of systematic reviews with their clinical expertise and with patients’ preferences, bearing in mind that high quality scientific evidence does not take decisions, physicians and patients do.

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