

GUIDES TO UNDERTAKING RESEARCH

3.3 Systematic Reviews – A Short General Introduction

Clinicians need to know whether a treatment may be effective for their patient or, indeed, if it works at all. Published clinical studies are the main source of authoritative and objective information but there are problems in simply accepting these at face value: studies vary enormously in size and quality and may contain biases (i.e., systematic flaws) that undermine their conclusions. To make matters worse, there is the particular problem of publication bias, which means that not all studies are published. Thus, for example, exciting first data on an innovative therapy may be published with fanfare, while later boring studies showing that the therapy is useless struggle to be published at all. As a result, unsuspecting clinicians performing literature searches see only the good results and so can be badly misled. These problems can, at least in principle, be dealt with by systematic reviews.

Unsystematic reviews

A 'literature review' conventionally refers to an article that paints a detailed picture of the general current state of knowledge and thinking in a field. It is always supported by an accompanying extensive list of cited papers, bibliographies that are themselves useful resources. Such reviewing has a long and honourable history, but in recent years has emerged the more specialised and focussed type of article, the systematic review; the older type of review is sometimes referred to as a "narrative" review to contrast it.

What are they for?

A systematic review seeks to provide a direct answer to a focussed clinical question, and assess the strength of evidence that supports that answer. The question addressed may be simple but narrow, such as whether a specific treatment is effective for a particular category of patient. Secondary questions, such as optimal dose or the frequency of complications may also be addressed. Systematic reviews promote evidence-based medicine as championed by the Cochrane Organisation, a resource supported by medical institutions worldwide, and are regarded as a very high level of clinical evidence.

What is systematic about it?

Scientific endeavours are all systematic in some sense, but here it means the whole review process

itself is systematic, not just its methods and analyses. It follows a set of prescribed and standardised procedures. For example, a systematic review performs meticulous and exhaustive searches for *all* accessible clinical studies that address the question in hand, and details of that search process are declared. This includes studies found outside of standard journals or in languages other than English; this helps to overcome publication bias.

How is a systematic review performed?

That subject takes up entire books, with many aspects still quarrelled over. However, the general conduct of a gold standard systematic review is widely agreed.

A systematic review is performed using a transparent, orderly process to identify and assess relevant published studies. It weighs the evidence from those studies to reach a considered statement on the subject of enquiry. The systematic reviewing protocol is first designed, registered and published (accessibly) so that the review can later be seen to conform to the original intent, removing temptations to 'improve' the design later. All pertinent studies are then located, and a pair of researchers filter out those insufficiently relevant or informative; this filtering process is itself described in the review manuscript. The selected studies then

undergo evaluation of their scope, quality, biases, conclusions and soundness of their conclusions.

What is done with this information?

The outcomes and information from the reviewed studies are synthesised to reach a nuanced conclusion for which the studies provide support. There is an assessment as to whether the evidence is strong enough to be acted upon in the clinic, whether further studies are desirable and whether further issues are raised, such as the consistency of the therapy outcomes.

Is all that effort really needed?

The reviewing process is time consuming but is needed because the biases and problems quality affecting the studies must be exposed to daylight and critically evaluated. This facilitates good integration of information to enable rational clinical decisions.

Developing a systematic review uses many tiresome and tedious techniques but demonstrably and drastically reduce bias. It is part of human psychology that biases are underestimated and ignored. A key objective of evidence-based methodology is to overcome this dangerous tendency, although such efforts are rarely glamorous. There is good evidence, for example, that studies that do not have fully blinded patient allocation to treatment and placebo arms display measurably more systematic bias and error. Note also that a systematic review can be regularly updated (i.e., repeated) as more studies are performed, leading eventually to consensus on best practices.

What types of studies are included in the systematic review?

All relevant published data and grey literature, suitably filtered. 'Grey' literature refers to studies not formally published in conventional journals, such as published abstracts and conference presentations, non-peer-reviewed manuscripts

(e.g., bioRxiv) and studies not published in English. It is challenging to find and interpret such studies but it is a vital task.

What about meta-analyses?

A meta-analysis goes a step further than a systematic review as it takes published data and aggregates and appraises it with a number of statistical tools to reach conclusions based on quantitative analysis. This is a powerful method that can result in strong conclusions if the studies under scrutiny are under- or poorly-powered small studies, so can provide stronger evidence than the individual studies alone as long as biases are recognised and dealt with.

What happens if the studies that the systematic review reviews are no good?

Aggregation of information from badly executed studies cannot magically produce good data. However, aggregating weak or underpowered studies can, if coupled with the techniques of meta-analysis can provide stronger evidence than the individual weak studies can. Part of the systematic process is to weigh the quality of the studies. Good data with low bias from large studies contributes more to review conclusions than data from a poorly executed and wobbly study with few participants.

How are the biases and other flaws in studies assessed?

The standardised methods used to reduce bias cannot easily be summarised here, but common approaches include standard checklists (e.g., to assess the quality of randomisation and blinding) or quantitative measures such as funnel plots that assess publication bias. Such particular methods are selected beforehand then used rigorously and with great care.

In sum, a well performed systematic review is a crucial and high quality contribution to evidence-based healthcare.

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