

Systematic Reviews



One of the biggest challenges within scientific research is to interpret the results of individual studies in the context of other research that has been done. This is especially important for decisions about whether a medical treatment works and for decisions about what further studies should be done. For example, if a recent small study appears to show that a treatment works or a substance causes harm, but previous good-quality studies had concluded the opposite, these results need to be looked at together. If we don't do that, the dangers are:

- We can flip flop between opposing conclusions, as with press stories about chocolate or red wine being good for you or whether statins do or do not cause strokes.
- People can take notice only of studies that fit with their views, as with claims that homeopathy works, or that mobile phones cause cancer.
- We can fail to recognise hard-to-spot risks or benefits, which in fact show up clearly and quickly by combining studies.
- People can end up funding and conducting research that has already been done, which is wasteful and unethical particularly if it involves medical trials using human subjects or animal research.

The evidence from a number of studies can be gathered together in one report which pools and analyses all available data to assess the strength of the evidence.

These reports are **systematic reviews**.

Systematic reviews can:

- **End confusion**
A systematic review pooling data from 24 conflicting studies on statins found no evidence that these drugs increase stroke risk and in fact strong evidence that they prevent strokes.
- **Highlight where there is not enough evidence**
A systematic review on tonsillectomy as a treatment for throat infections showed no proper clinical trials had been done on adults so there was no good evidence arguing for or against this potentially dangerous surgery.
- **Yield new insights by combining findings from different studies**
Combining findings from studies on cot death and baby sleeping positions from different countries would have changed much earlier the standard dangerous advice to place babies on their front.

- **Show when enough evidence has been produced**

A systematic review would have shown clear evidence that the drug aprotinin reduces bleeding in surgery after 12 trials and would have prevented a further 52 unnecessary trials.

- **Reduce the influence of any flaws or errors in a single study**

A flaw in a study is a problem in its methods that may affect its outcome, making its conclusions wrong or suspect. For example, the people running a drug trial might give the drug only to the healthiest volunteers. Researchers might apply the methods inappropriately, for example by only including data from volunteers who responded well to the treatment.

How systematic reviews are carried out.

Systematic reviews are scientific studies so they must use scientifically rigorous methods.

All of the available evidence to answer a specific well-defined research question must be identified. Researchers must search all sources of published studies and consult scientists in the field for any unpublished studies. Sometimes studies that do not show an effect or show a negative result are not published as promptly as those that do – this is called publication bias – but these studies are essential for a systematic review and should be sought out and included.

Authors of systematic reviews have detailed quality control guidelines for studies because not all studies are of equal quality and some studies contain flaws. The guidelines are agreed before beginning the review – they must be clear and precise and applied to all the studies found. Studies that do not satisfy these guidelines are rejected.

Does excluding studies from a systematic review make it weaker?

People who disagree with the conclusion of a systematic review often criticise it for ignoring relevant evidence. It may seem counterintuitive to set out to eliminate apparently relevant studies from a systematic review because more studies mean more participants, which will reduce the play of chance. However, it is essential to evaluate the methodological quality of a potentially eligible study before it is included; if studies with poor methodology are included in a review then their misleading results might distort its conclusion. This is more important than simply getting more data.

This is illustrated in a systematic review by Shang *et al* (2005) on homeopathy. This systematic review was widely reported and discussed and it was attacked by supporters of homeopathy for 'ignoring most of the evidence' in its favour.

The authors searched thoroughly for placebo-controlled trials of homeopathy (where homeopathy is tested against a dummy medicine) using electronic databases and contacts with experts in the field. They found 110 homeopathy trials looking at several different disorders and then selected 110 conventional medicine trials looking at the same disorders and measuring the same outcomes. When they initially examined the data from all these trials they found there was evidence for effectiveness of the treatment beyond the placebo effect both for homeopathy and for conventional medicine.

The authors then applied their control guidelines for studies, which they had defined before the beginning of the systematic review, and excluded all trials which did not fulfil their guidelines. They looked for:

- Randomisation – participants in the trial should have been allocated completely at random to the treatment and control groups
- Blinding – neither the participants nor the therapist nor anyone analysing the data in the trial should have known to which group a participant had been allocated
- A comprehensive written report of the trial had to have been available with adequate data on all participants in the trial
- A large enough number of participants in the trial

Excluding all the poorer quality trials left only 8 good quality homeopathy trials and only 6 good quality conventional medicine trials. Analysis of these showed there was no evidence that homeopathy has any effect on the disorders beyond the placebo effect.

However even after being subjected to the same rigorous scrutiny and elimination of poor quality trials, treatment by conventional medicine was still found to have been effective compared to placebo.

What you need to know about a systematic review	
Not everything with 'review' in the title is a systematic review	It needs to be an analysis of evidence and not just be a literary review talking of selected studies
A systematic review should answer a particular defined research question	The question needs to be defined precisely, including carefully defining the population and the relevant outcome, so that the studies included are appropriate and comparable with each other
It was carried out with scientific rigour	Complete methods will be available detailing comprehensive searching for all the evidence and the authors' quality guidelines. Every decision they made should be transparent. Conflicts of interest, or lack of them, should be declared.

Systematic reviews are better at assessing strength of evidence than single studies.

They are vital in health care:

- they save lives by highlighting the best treatments and identifying those that are unproven or harmful.
- they save money by indicating when enough research has been done.
- they help prevent unethical studies by avoiding duplicate or unnecessary animal and human trials.

Choosing studies for inclusion in a systematic review is not a personal or political decision but based on scientific reasoning.

Further information:

The Cochrane Collaboration is an international not-for-profit organisation that provides up to date systematic reviews in healthcare topics carried out by their volunteer scientists and academics. www.cochrane.org

The James Lind Library was established to help patients and clinicians understand fair tests of treatments in healthcare. www.jameslindlibrary.org

Testing treatments: better research for better healthcare. Evans I, Thornton H, Chalmers I. London: British Library, 2006. A PDF of this book freely available under a Creative Commons Licence through www.jameslindlibrary.org

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