

Systematic reviews help users keep up with expanding volume of research evidence

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The future holds the promise of continued expansion of the body of research information. However, it also holds the parallel threat of increasingly inadequate time and resources with which to find, evaluate, and incorporate new research knowledge into everyday clinical decision-making. Fortunately, mechanisms are emerging that will help us acquire the best, most compelling, and most current research evidence. Particularly promising in this regard is the use of systematic reviews.

– from an editorial in the
Annals of Internal Medicine, 1997 126:5

The current push towards evidence-based decision-making has created a tremendous challenge for clinicians, workplace parties, policy-makers and others involved in workplace health and illness.

Every year six million new articles reporting the results of biomedical research are published by scientists around the world. But how does this new information fit into the context of existing research? How can users be sure that the researchers' conclusions are scientifically valid?

This is where the systematic review – a highly specialized type of research in itself – can be extremely useful, says Dr. Anthony Culyer, Chief Scientist at the Institute for Work & Health (IWH). “The systematic review is a short-cut for those who want to keep up on the latest research but can't regularly comb through journals and databases,” he explains. “It delivers a concise and relatively

unbiased synthesis of the research evidence which busy people can apply in their own decision-making.”

For more than 25 years, systematic reviews have been used – mainly in medicine – to provide evidence about the usefulness of various diagnostic tests and treatments, for example. More recently, however, researchers in other fields such as economics have started exploring the potential of doing their own systematic reviews.

What are we talking about?

Different terms are used to describe the process of reviewing and synthesizing scientific literature, and this can be confusing for researchers and non-researchers alike:

- A systematic review uses strict methods to identify, select and critically appraise relevant studies on a certain topic. This is done to prevent or limit errors and also to make the results of the review more transparent to those who will use the findings.
- When researchers statistically combine results from two or more studies, this is called a quantitative review or meta-analysis.
- When researchers summarize their findings but do not statistically combine results from two or more studies, this is called a qualitative review.
- A research summary that lacks clearly defined and explained methods is called a narrative review (sometimes called research synthesis and overview.)
- Other “integrative” products like clinical practice guidelines, economic evaluations, and clinical decision analyses often incorporate the results of systematic reviews.

Most people, including many researchers, don't appreciate the time, resources and skills needed to produce a high-quality systematic review.

"Researchers routinely spend hundreds of hours searching through thousands of citations in various computerized databases, looking for studies pertaining to their topic," says Dr. Andrea Furlan, a physician who is the Institute's Evidence-based Practice Coordinator. "But this is just the first step in a much longer process."

To understand the value of a quality systematic review, you must understand the potential advantages that flow from this type of research. "We do more than simply search out studies on a particular topic, review the evidence and describe what we found," Furlan says. For example, reviewers may locate several trials of a particular drug or intervention carried out by different researchers, each involving 50, 75, 100 or 200 subjects. Such relatively small sample sizes may mean the study findings lack "statistical power" – that is, not enough patients were studied to accurately determine whether the intervention was effective or might be effective for other groups of similar patients.

"But if the studies are similar enough, we can pool the numbers in such a way that we get, in effect, one large sample of 600 patients, which increases statistical power," Furlan explains. "This may allow us to see effects – positive or negative – that weren't captured in the smaller original studies."

Software and skills

In the past, researchers doing systematic reviews were limited to "hand-searching" – reading tables of contents in journals and photocopying potentially relevant studies.

More recently, sophisticated computer tools and software have been developed to help reviewers find studies, manage the references and data and carry out complex statistical analyses, explains Emma Irvin, Manager of Library and Information Systems at IWH. "These tools and software may reduce the overall costs of doing systematic reviews and improve the review process so there's less room for error," she adds.

The skills needed to carry out a good systematic review vary with the topic. A review that focuses on illness prevention, diagnosis or treatment would likely require expertise from a physician or other clinician in that area. But the skills of epidemiologists, statisticians, economists, librarians and others may also be needed.

"The Institute has a pedigree in doing systematic reviews of the workplace health literature, usually as a first step in our own research projects," says Chief Scientist Culyer. "It's also a good way to generate primary research – the process identifies gaps in the literature where quality research is desperately needed."

Each year Institute researchers publish a number of systematic reviews, and this activity is expected to increase. "New funding from the Workplace Safety & Insurance Board of Ontario will allow us to expand our systematic review activities over the next four years," says Institute President Cameron Mustard.

"The main focus will be systematic reviews of the literature in the area of workplace injury prevention."

Who uses systematic reviews?

Systematic reviews are now being used by many people involved in the health-care system:

- Those who seek the best evidence to inform their thinking, decision-making, and practice include health-care professionals, patients, insurers, policy-makers, health-care advocates and health-care executives.
- Researchers use systematic reviews to identify gaps in knowledge about a particular question before planning further studies.
- Some national health-care systems and private health plans now routinely require systematic reviews on a topic before deciding whether to pay for expensive new therapies.

"This may explain the virtual explosion of systematic reviews now taking place in the research community," says Victoria Pennick, who coordinates the work of the Cochrane Collaboration Back Review Group which is housed at the Institute. One 1997 survey found that the number of reviews produced annually had increased 500-fold during the previous decade.

Results may be contradictory

Systematic reviews can't solve every question: when it comes to many complex topics, good reviews are either lacking or can't be used. Reviews have other limitations, too, explains Dr. Claire Bombardier, an IWH Senior Scientist, Co-editor of the Back Review Group and Professor of Medicine at the University of Toronto.

“It’s not unusual for different reviews to reach contradictory conclusions on the same question,” she says. “Part of the problem is that reviewers may have included low-quality trials in their review or done statistical pooling when this was not appropriate.”

While high-quality reviews can help many users of research evidence, she says, “clinicians must always combine such evidence with clinical judgment, their knowledge of each patient and the patient’s own preferences.”

In 2003 the Institute began tapping its own expertise to teach others the art and science of systematic reviews – how they are done, how to distinguish a good review from a poor one, how to understand the findings and how to get started doing systematic reviews. Dozens of researchers, academics, nurses, clinical epidemiologists, students and private sector representatives have already attended these workshops, and more are planned.

“We have been surprised and gratified at the interest,” says Furlan who helped develop, organize and teach the workshops. “In fact, there were waiting lists for a number of these sessions, so clearly there’s a lot of interest in systematic reviews out there.”

Anatomy of a Systematic Review

When it comes to scientific studies, the systematic review doesn’t possess the somewhat “glamorous” reputation of the randomized controlled clinical trial – a type of research that tests ways to diagnose, treat and prevent disease.

But while a systematic review is very different from clinical research, the process can be every bit as time-consuming, painstaking and challenging. “The concepts and techniques involved ... are at least as subtle and complex as many of those currently used in molecular biology,” according to a 1997 editorial in the *Annals of Internal Medicine*.

To explain and demystify the subject, here is a highly simplified, step-by-step description of the systematic review process, using a recently published systematic review as our example. (see “Sample systematic review on muscle relaxants” on page 000).

STEP 1: Decide on an appropriate topic and then develop the review question

Systematic reviews can be designed to answer a range of questions from “What is the effect of therapy A on people with a particular health problem?” to broader policy and

management issues affecting the organization or delivery of health services.

First, scientists usually seek to establish such research is needed by doing a quick scan of the existing literature. Here, for example, they were satisfied that no high quality, recent review of muscle relaxants for low-back pain already existed.

Sample systematic review on muscle relaxants

Title

Muscle relaxants for non-specific low back pain. Published in *Spine* (2003, Volume 28, Number 17 page 1978–92)

About the review

The review detailed was carried out by Institute Adjunct Scientist Dr. Maurits van Tulder and PhD Student Dr. Andrea Furlan. Other team members were Dr. Tony Touray, Dr. Lex Bouter and Sherra Solway. The review was done under the auspices of the Cochrane Collaboration Back Review Group which is housed at the Institute for Work & Health. The Collaboration is an international research organization that specializes in systematic reviews of the health literature.

About the findings

The review found strong evidence in the scientific literature that muscle relaxants were more effective in providing short-term relief from acute low-back pain than placebos or dummy drugs. But side-effects like dizziness and sedation were “significantly more prevalent” in patients who took muscle relaxants for this purpose. The evidence showed no single drug in this class was superior to the others.

In this case, the review question – “Do muscle relaxants reduce pain and disability in people with non-specific low-back pain?” – focused on a specific population and setting (people with non-specific low-back pain seeking medical treatment) and described the outcomes of interest (relief from low-back pain, return to normal activities and side effects from medication.)

STEP 2: Develop a search strategy then carry out the literature review

During this stage, so-called “inclusion” and “exclusion” criteria – a strict set of rules about whether particular characteristics of each study make it a good candidate for the review – are developed.

Then reviewers begin the enormous task of searching the literature. This usually involves entering explicit search terms into electronic databases and hand-searching older journals. They must also diligently search out other sources of data including unpublished studies, known as the “grey literature.” (Research shows that a review which relies only on published trials can end up overestimating the benefits of health-care interventions.)

In this case, the reviewers did a computer-assisted search of studies published in English, Dutch, German, Spanish or Portuguese that were listed in three major electronic databases: MEDLINE, EMBASE and CENTRAL.

As each study was identified, two reviewers independently screened the title and abstract (summary) to see if it met the inclusion criteria. After this initial screen, the full text of each selected paper was evaluated independently by two Review Team members to verify that the study was acceptable. In the end, 30 trials met the inclusion criteria.

STEP 3: Extract data from the studies included in the systematic review

Every systematic review includes a concise summary of each relevant study. This information is usually provided in the form of a “summary table” or “evidence table.”

Here, the reviewers “pulled out” and compiled information from each chosen study – for example, demographic information about patients, including their age and gender; data about their symptoms, the kinds of muscle relaxant drugs prescribed during the trials, and any improvement in symptoms and/or any side effects reported by participants. All information extracted from the 30 studies was stored in a specialized computer database.

STEP 4: Combine data from the studies using proven statistical methods and software

The objective of most systematic reviews is to provide a reliable estimate of the effects of an intervention – in this case, the use of muscle relaxants for low-back pain. This

is usually achieved by “synthesizing” or combining data from many studies where it is appropriate to do so.

First the reviewers must decide what kind of synthesis is best-suited to their findings. If relevant, valid data are lacking, or if the individual studies are statistically too different, then quantitative synthesis should be avoided. Instead, reviewers are advised to carry out a qualitative synthesis – looking at individual study findings, then grouping and reporting on them in a narrative fashion.

The reviewers must clearly describe and document their approach to data synthesis. In this case, the Review Team carried out both qualitative and quantitative analyses of the trials on muscle relaxants and low-back pain.

STEP 5: Place the review findings into a useful context for the intended audience

Once they understand the data, the reviewers must think about “context.” Were they able to answer their original question? How good was the quality of the studies included in the review? How confident are they about the results? Was there any chance that the results might be biased? What do the findings mean to potential users?

Reviewers should also do a “risk vs. benefit” analysis – do the potential benefits of an intervention outweigh any harms? They may also discuss whether the cost of a treatment or intervention is worth the possible benefits. In this case, the reviewers wondered whether the generally positive findings about muscle relaxants could be related to the fact that almost all the studies were sponsored by drug companies.

In the review of muscle relaxants, the Review Team concluded that patients who took them were more likely to obtain relief from low-back pain than those who got placebos. But these improvements tended to be relatively modest, suggesting clinicians and patients must weigh them against the increased risk for side effects such as dizziness and sedation.

STEP 6: Report the results and conclusions

Writing up the results of a systematic review is both an art and a science. Once the Review Team decides how to interpret the results, usually one person writes the first draft, ensuring it meets the basic requirements for reporting such research.

In this case, the first draft was shared with all members of the Review Team who made suggestions. The paper

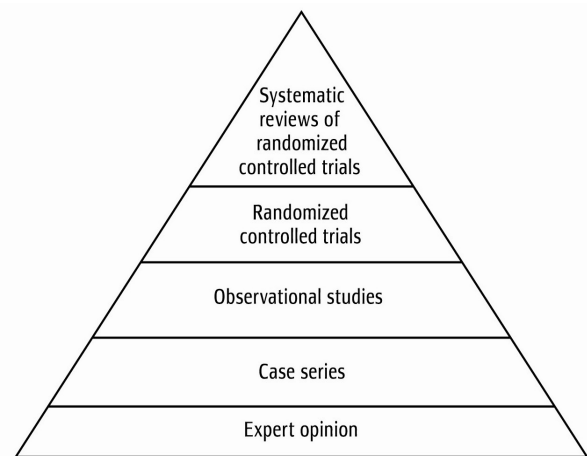
How strong is the evidence?

How reliable is the information produced by a systematic review of the literature? It depends on how carefully the review was done and on the quality of studies included.

A well-designed systematic review of randomized controlled clinical trials sits at the top of the “best evidence” hierarchy, according to this model developed by the Centre for Evidence-Based Medicine at Oxford University in England.

However, many research questions – those concerning certain kinds of workplace interventions, for example – don’t lend themselves to randomized controlled trials.

In these cases, reviewers must select observational studies or case series.



was then revised and sent out for a second review. The final draft, including tables and graphs, was submitted to the Cochrane Back Review Group editorial board which then requested further revisions. Then, the review was approved for publication in the Cochrane Library and co-published in the journal *Spine*.

The goal of publishing this systematic review was to share evidence-based knowledge with physicians and other clinicians who treat low-back pain. The findings may help guide them as they talk to patients about the risks and benefits of muscle-relaxant drugs which are widely marketed and used for low-back pain.

Need more information about systematic reviews?

You can access an excellent article about systematic reviews written for a non-scientist audience by renowned science journalist Ray Moynihan. The article, entitled “Evaluating Health Services: A Reporter Covers the Science of Research Synthesis,” was published in 2004 and appears on the web site of the Milbank Memorial Fund, an endowed U.S. foundation that engages in nonpartisan analysis, study, research and communication on significant issues in health policy.

<http://www.milbank.org/reports/2004Moynihan/040330Moynihan.html>

The following web sites provide detailed information about systematic reviews and the role they play in evidence-based practice:

Bandolier

www.jr2.ox.ac.uk/bandolier/index.htm

Produces updated information for clinicians, patients and others in the form of systematic reviews, meta-analysis, randomized trials, and high-quality observational studies.

Canadian Coordinating Office for Health Technology Assessment

<http://www.ccohta.ca>

Provides the public with information about health technologies, focusing on evaluations of clinical effectiveness and cost-effectiveness.

The Cochrane Back Review Group

<http://www.cochrane.iwh.on.ca/>

The Cochrane Back Review Group coordinates international reviews of literature on primary and secondary prevention and treatment of neck and back pain and other spinal disorders.

The Cochrane Collaboration

<http://hiru.mcmaster.ca/cochrane/default.htm>

Relying on the work of more than 10,000 people around the world, the collaboration has produced almost 2,000 systematic reviews.

Health Evidence Network (HEN)

<http://www.who.dk/eprise/main/WHO/Progs/HEN/Home>
Within the World Health Organization (WHO), HEN is an information service primarily for public health and health-care decision-makers in the WHO European region.

Informed Health Online

<http://www.informedhealthonline.org>
Provides information and resource tools that helps the public keep up-to-date on the effects of healthcare.

National Health Service Center for Reviews and Dissemination

<http://www.york.ac.uk/inst/crd/>
This group at the University of York in England provides research-based information about the effects of interventions used in health and social care. It conducts systematic reviews as part of its work.

National Institute for Clinical Excellence

<http://www.nice.org.uk>
Within the publicly funded National Health Service in England and Wales, NICE provides the public with information on “best practices” and commissions systematic reviews.

A sampling of systematic reviews about back pain and workplace health

Here are some of the systematic reviews involving scientists and students at the Institute for Work & Health:

Recently published systematic reviews:

The use of back belts for prevention of occupational low back injuries (Published 2003) C Ammendolia et al

Updated Cochrane review: massage for low-back pain (Published 2002) A Furlan

Multidisciplinary rehabilitation for chronic low-back pain: systematic review (Published 2001) J Guzman et al.

A critical review of reviews on the treatment of chronic low-back pain (Published 2001) A Furlan et al.

Updated Cochrane review: Acupuncture for low-back pain A Furlan et al (Published 2005)

Systematic reviews completed, awaiting publication (Some executive summaries available on IWH web site)

Workplace-based return-to-work interventions
RL Franche et al.

The effectiveness of participatory ergonomic interventions D Cole et al.

The effectiveness of occupational health and safety management systems L Robson et al.

Systematic review of the prevention incentives of insurance and regulatory mechanisms for occupational health and safety E Tompa et al.

Exercise for work-relevant neck pain G van der Velde et al.

Systematic reviews currently in progress

Cochrane review: Traction for low-back pain J Clarke et al.

Updated Cochrane review: Exercises for low-back pain J Hayden et al.

A systematic review of risk factors for work injuries among youth C Breslin et al.

A systematic review of dynamic radiography in non-specific low-back pain C Ammendolia et al.