

How to Perform a Systematic Literature Review

A Guide for Healthcare
Researchers, Practitioners
and Students

Edward Purssell
Niall McCrae



Springer

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Introduction

1

The field of healthcare has undergone, and will continue to undergo, rapid change. Recent events have shown the importance of sharing and understanding data and the need to respond quickly to events. In a hyperconnected world in which a virus can spread throughout the continents in weeks, we no longer need to wait months for print journals to deliver important research findings. Fortunately, we have, in the form of the internet, a tool that enables knowledge to travel around the world at an even faster pace than even the most contagious virus. Quicker and wider access to information, alongside greater transparency in research conduct, should lead to a golden age of evidence-based practice.

However, this information must be managed. The internet is a double-edged sword, as false or dubious claims spread quickly and threaten to undermine the good work of clinicians and researchers, misleading the public and possibly practitioners too. Furthermore, when making decisions that can quite literally be a matter of life or death, it is important that those making these decisions do so using the best available knowledge and also that as knowledge changes so does policy. Acting on partial or poorly understood information can have devastating effects on communities and individuals. When considering a problem, there is always the temptation to use a search engine and read only the first study that comes up; this would not only be lazy, but risky.

The World Health Organization declared the coronavirus (Covid-19) to be a pandemic on 12 March 2020. There was a need for much new research into the control and treatment of Covid-19; but there was also a need to have a good understanding about what was already known. Wasting valuable time and resources on replicating existing knowledge is not acceptable in any circumstances, least of all in this situation. Already by 6 April 2020, one of the main control measures, that of school closures, was critically examined in a rapid systematic review of school closures and other school social distancing practices across the world [1]. Such a review is far more useful to policy-makers and the public than looking at original studies, many of which will be behind paywalls and so inaccessible to most people and who also may not understand the methodological and statistical details of the papers

even if they did have the time and inclination to read them all. This is the role of the systematic review.

One example of what can go wrong, with devastating consequences, was with the measles, mumps, and rubella (MMR) vaccine. One ill-judged case series that suggested a link between the MMR vaccine and autism, subsequently retracted [2], was the basis for a rumour that reduced public confidence in the vaccine to such an extent that many parents refused to have their children vaccinated. As a result of this, we saw epidemics of diseases in places where they were thought well controlled. Had people been able to look not just at the one study but the entire body of literature the lack of evidence for this association, this might have been avoided. Actually, the work of the reviewer entails looking critically at the literature, in this case recognising the inherent weaknesses of the case series as a form of evidence and other clues perhaps to the veracity of any claims [3]. In pointing this out, we are not saying that the case series is a flawed methodology, just that it can never show cause and effect. To see the correct use of a case series like this, we might look at a paper in the American Morbidity and Mortality Weekly Report from 1981, which reported the cases of five apparently healthy young men with *Pneumocystis pneumonia*. This was interesting because this condition is very unusual, and to see so many cases in apparently healthy people was unknown. We now know that they were the first reported cases of acquired immune deficiency syndrome (AIDS). However, starting the findings, the conclusion though is appropriately measured: ‘All the above observations suggest the possibility of a cellular-immune dysfunction related to a common exposure that predisposes individuals to opportunistic infections such as pneumocystosis and candidiasis’ [4].

Because they use the entire body of literature, systematic reviews are widely regarded as the highest form of evidence by the scientific community. Rigour and replication are the bedrocks of science. In this regard, review methodologies have undergone enormous change in recent years, indeed during the period over which this book has written new tools and techniques have become available. The days of a systematic review being comprised of a few papers you have hanging around plus a quick search are long gone! As we emphasise throughout this book, a review should produce a whole greater than the sum of parts. Whether the reviewed studies are quantitative or qualitative, the output is more than a summary; a distinct contribution to knowledge is made by interpreting the weight and meaning of evidence.

The above requirements mean that writing a systematic review requires a team that usually encompasses subject experts, at least one person who is knowledgeable about literature search strategies, systematic review methodologists, someone experienced in the methods used to analyse the data and a team to write the review. Our own contributions to the systematic review literature have encompassed mental health [5, 6], infection control [7] and child health [8, 9].

It is important to stress that systematic reviews cannot be conducted on every topic, and in some areas, it is more difficult than others. It relies on the question being amenable to research; not all are. It relies on literature being available. It also relies on a sensitivity to and understanding of the difficulties of the primary

researchers. Research can be a long, frustrating and lonely business; reviewers should always remember this when reviewing the work of others.

For budding systematic reviewers, we hope that this book will inform and inspire you. We also hope that it helps experienced reviewers and academic supervisors to reconsider some of their assumptions. We are all learning all of the time, and this book is certainly not the last word, but we are confident that our guidance will keep you on the right track, heading in the right direction.

1.1 How to Read This Book

Although a systematic review has distinct parts, they only really make sense as a whole; one part informs the next. We suggest that you read each chapter as you go along. Each chapter can be used individually, but it may require some flicking back and forth between chapters. We have indicated in the text where this may be needed.

All of the references are in a Zotero Group; you can access this here: <https://www.zotero.org/groups/2460528/systematicreviewbook/items/APGI5B9K/library>.

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A Brief History of the Systematic Review

2

Summary Learning Points

- The concept of evidence-based practice is not new, but it has been inconsistently applied in practice.
- Systematic review methodologies have developed over time and will continue to do so. This means that reviews conducted some years ago will often have different reporting and methodological qualities to those done today.
- Review methodology changes frequently, and it is important that those teaching and conducting them stay up to date with current practices.
- Systematic reviews should be treated as any other kind of research, and it is important to recognise their limitations as well as their strengths and to be measured when making claims of causation.

2.1 Literature Past and Present

Let us contrast nursing and medicine in how they read research. Most nurses in current practice received their education at university, having entered the professional register with a degree. Until the late twentieth century, however, nurses were trained in a hospital-based school of nursing, near the wards and their living quarters (in some hospitals, the school occupied the ground floor of the nurses' home). Traditionally, training was an apprenticeship, with little academic demand. Recruits had chosen a practical discipline—and discipline it was, with strictly enforced rituals and routine. In a gendered division of labour, the good (female) nurse was neatly groomed, diligent and obedient to (male) doctors.

Examinations and essays during training were handwritten, with no requirement for references. The library of a typical school of nursing held collections of the weekly *Nursing Times* and *Nursing Mirror* magazines, alongside standard textbooks on anatomy and various fields of nursing practice. Controversy was scarce, because all nursing schools provided the same information, and uncertainty about diagnoses or treatments was rarely debated. Instead of the multidisciplinary ethos of today, most reading material was specifically for nurses, and nursing knowledge was

predominantly about care rather than treatment. Consequently, nursing students and fledgling nursing researchers learned to make do with a limited array of literature. To some extent, this disciplinary isolation persists in the notion of ‘nursing research methods’.

Medical libraries were on a higher academic plane. Trainees delved into peer-reviewed journals, which filled the shelves from floor to ceiling. Annual volumes of the *Lancet*, *British Medical Journal* and a plethora of specialist publications were collated in bespoke binders; new editions were placed on a rack for ready access. Whereas books were soon outdated, journals presented the latest available research findings (albeit months after the authors had completed their study). Three or four decades ago, there were considerably fewer journals, and it was possible for trainees or researchers in better-endowed medical schools to complete a fairly thorough literature review over a few days in the library. Indexes of literature existed in the predigital era but were cumbersome and infrequently updated. Writers often relied on reference lists to find relevant papers. Interlibrary arrangements enabled retrieval of papers from journals held elsewhere, but there was often a long wait for photocopies from elusive sources.

Students have less need to visit a library today. Paper copies are no longer published by most journals, and the accumulated binders from earlier decades have disappeared from the modern electronic library, which mostly exists in virtual form on an intranet. Literature searches are automated, using bibliographic databases such as Medline. However, not all universities have the same resources, as online journal and database subscriptions are expensive (like pubs that show live football matches, libraries pay much higher fees than charged to an individual subscriber). To use cable television as an analogy, the premier seats of learning, such as the Russell Group universities in the UK or the Ivy League in the USA, purchase the full package with movies and live football, while the former polytechnic colleges are restricted to news channels, soap operas and quiz shows.

Meanwhile, the academic publishing system is changing radically. Increasingly authors are paying for readers to have open access to their papers, thereby maximising readership and impact. Sooner rather than later, this will become the only way to get published in journals. Healthcare knowledge is apparently being liberalised, but there are pitfalls in this progressive venture. The typical fee of around £2000 (\$2500) should be included in the study funding application. Fees are likely to increase after the current transitional phase, as academic publishers will depend on researchers for income. However, not all studies are funded. Consequently, small-scale qualitative studies, which can be useful primers for more substantial research, might be inhibited. Literature reviews, which may be a product of students’ dissertations or ad hoc projects by faculty staff, could also be curtailed by publication costs. Nursing has tended to receive a smaller ‘slice of the cake’ in research funding, and the new business model could perpetuate power imbalance towards privileged institutions and professions.

The peer-reviewing model continues as before, but a growing number of journals are competing for a limited pool of expert reviewers. Business interests might influence publishing decisions: journals need papers to survive. There is danger of

quantity undermining quality, as new or obscure journals offer novice writers certainty of publication (for a price). As soon as a writer gains a publication record, he or she will be bombarded with unsolicited requests from predatory journals to submit a paper. Unwary readers who stumble across this terrain are exposed to poorly conducted and inadequately reviewed studies. Many of these titles will not be indexed by research databases. In their pursuit of evidence from all valid sources, literature reviewers should be aware of these trends in publishing and any inherent loss of quality control or bias.

Literature reviewing is in some ways easier and in other ways more challenging than in the past. Everything now is digital and increasingly accessible. The process of reviewing has developed, with established rules for performing and reporting. Scientific standards have been raised in the form of the systematic literature review, which has become the prime information resource for healthcare practitioners. However, a plethora of tools and checklists might seem more of a hindrance than a help.

2.2 A Man with a Mission

Although he was not the first to call for a stronger scientific basis to healthcare, Archibald (Archie) Cochrane is justly honoured as the architect of evidence-based practice, and his life story is worth telling. Born in Galashiels, Scotland, in 1909, Cochrane had porphyria at birth, a condition that influenced his professional career [1]. Gaining a place at the University of Cambridge, on graduation in 1931, he became a research student in a tissue culture laboratory. Dissatisfied with this work, he moved to Germany to study psychoanalysis under Theodor Reik, who had been one of Sigmund Freud's first students. Reik fled persecution by the Nazi regime, and Cochrane followed him to Vienna and then to the Netherlands. In his own analysis by Reik, Cochrane discussed a sexual problem that he attributed to his porphyria. However, he derived little benefit from such therapy, and he concluded that psychoanalysis lacked scientific basis.

Cochrane began medical training, which was interrupted by the Second World War. He enlisted but was captured in action by the Germans. As a prisoner of war, his modest grasp of German language and his medical proficiency gained him a dual appointment as medical officer and negotiator. He conducted a dietary trial and persuaded the camp administrators that a yeast supplement would cure the widespread problem of oedema among inmates. After the war, he completed his training at the University College Hospital in London and undertook specialist training in epidemiology, an emerging branch of medical science that explores the causes of disease by statistical rather than laboratory methods. Cochrane worked in a research unit on pneumoconiosis, which was a particular health hazard in the massive workforce of coal miners. This led to a professorship of tuberculosis in Wales. He was also appointed as honorary director of the Medical Research Council Epidemiology Unit, where he introduced a grading scale for response rates in studies (a rate of 91% scored 1 'Cochrane units', 95% scored 2 units; less than 90% was deemed unacceptable).

Awarded a fellowship by the Nuffield Provincial Hospitals Trust, Cochrane wrote an incisive review of the National Health Service (NHS). His short monograph *Effectiveness and Efficiency* [2] applied three measures: effectiveness (whether a treatment changes the course of a disease), efficiency (how well the NHS deployed resources such as staff and equipment to deliver an intervention) and equality (consistency of access to care and variation between hospitals). Cochrane was scathing of NHS medicine for its untested treatments and unfounded assumptions in clinical practice. Tonsillectomy, for example, was very frequently performed on children, but often without clear indication. Overtreatment entailed unnecessary hospital admission and surgery. By contrast, other medical conditions were undertreated, particularly in the elderly. Variation in care may be justified by individual patient's circumstances, but not by institutional discrimination.

Cochrane promoted randomised controlled trials (RCT) as the best evidence for any treatment. However, research often produced contrary results, as with the outcomes of tonsillectomy, and practitioners were unsure about which findings had most weight. Cochrane [3] remarked: 'It is surely a great criticism of our profession that we have not organised a critical summary, by specialty or subspecialty, adapted periodically, of all relevant randomised controlled trials'. By instilling a rigorous approach to understanding and applying empirical evidence, Cochrane's legacy was to integrate research and practice. By the turn of the millennium, the doctrine of evidence-based medicine was firmly established [4].

2.3 Hierarchy of Evidence

By the time of Cochrane's call for better evidence, the RCT had been in use in medical research for some decades. Experimental methodology was the vehicle for the tremendous growth of the pharmaceutical industry in the mid-twentieth century, as the marketing success of a new drug depended on convincing results. In clinical practice, however, prescribing by doctors was often based on untested assumptions. For example, until the 1950s, it was not unusual for patients suffering from anxiety or stress to be advised to smoke. The discovery of a causative link between smoking and lung cancer was a turning point in medicine, because it demonstrated the necessity for scientific investigation and evidence (although Cochrane himself was not deterred from his nicotine habit).

One of the most famous studies in the history of medical research was by Austin Bradford Hill and Richard Doll, who showed that smoking causes lung cancer. In 1947, the Medical Research Council (MRC) appointed a team of experts to investigate the troubling increase in incidence of this disease, and Bradford Hill was chosen following his work on tuberculosis, a wasting disease that had become known as the scourge of humankind. As a young man, Bradford Hill had been expected to follow his father's footsteps into medicine, but he was waylaid by tuberculosis [5]. There was no effective treatment, and like many thousands of other sufferers, he was sent to a sanatorium, where the disease was slowed by a regime of fresh air (beds were wheeled out to verandahs). Bradford Hill was treated by the surgical