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Chapter 1: Introduction

UNDER CONSTRUCTION - PLEASE DO NOT USE

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Key points

- Systematic reviews seek to collate all evidence that fits pre-specified eligibility criteria in order to address a specific research question.
- Systematic reviews aim to minimize bias by using explicit, systematic methods documented in advance with a protocol.
- Cochrane prepares, maintains and promotes systematic reviews to inform decisions about health and social care (Cochrane Reviews).
- Cochrane Reviews are published in the Cochrane Database of Systematic Reviews in the Cochrane Library.
- The Cochrane Handbook for Systematic Reviews of Interventions contains methodological guidance for the preparation and maintenance of Cochrane Intervention Reviews, Overviews of Reviews and Methodology Reviews.
- Methodological advice on Cochrane Diagnostic Test Accuracy Reviews can be found in the separate Cochrane Handbook for Diagnostic Test Accuracy Reviews.
- Cochrane has developed conduct and reporting standards.

1.1 Cochrane

1.1.1 What is Cochrane?

Trusted evidence. Informed decisions. Better health.

Cochrane is a global independent network of health practitioners, researchers, patient advocates and others, responding to the challenge of making the vast amounts of evidence generated through research useful for informing decisions about health (www.cochrane.org). Previously known as The Cochrane Collaboration, it is a not-for-profit organization where collaborators aim to produce credible, accessible health information that is free from commercial sponsorship and other conflicts of interest.

Cochrane's mission is to promote evidence-informed health decision-making by producing high quality, relevant, accessible systematic reviews and other synthesized research evidence. The work of Cochrane is underpinned by a set of 10 key principles, listed in Box 1.1.a.

Box 1.1.a: The 10 principles of Cochrane

1. Collaboration	by fostering global co-operation, teamwork, and open and transparent communication and decision-making.
2. Building on the enthusiasm of individuals	by involving, supporting and training people of different skills and backgrounds.
3. Avoiding duplication of effort	by good management, co-ordination and effective internal communications to maximize economy of effort.
4. Minimizing bias	through a variety of approaches such as scientific rigour, ensuring broad participation, and avoiding conflicts of interest.
5. Keeping up-to-date	by a commitment to ensure that Cochrane Systematic Reviews are maintained through identification and incorporation of new evidence.

6. Striving for relevance	by promoting the assessment of health questions using outcomes that matter to people making choices in health and health care.
7. Promoting access	by wide dissemination of our outputs, taking advantage of strategic alliances, and by promoting appropriate access models and delivery solutions to meet the needs of users worldwide.
8. Ensuring quality	by applying advances in methodology, developing systems for quality improvement, and being open and responsive to criticism.
9. Continuity	by ensuring that responsibility for reviews, editorial processes and key functions is maintained and renewed.
10. Enabling wide participation	in our work by reducing barriers to contributing and by encouraging diversity.

1.1.2 A brief history of Cochrane

The Cochrane Collaboration was founded in 1993, a year after the establishment of the UK Cochrane Centre in Oxford, UK. The UK Cochrane Centre arose from a vision to extend a ground-breaking programme of work by lain Chalmers and colleagues in the area of pregnancy and childbirth to the rest of health care. Inspired by Archie Cochrane's claim that "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" (Cochrane 1979), Chalmers and colleagues developed the *Oxford Database of Perinatal Trials* and a series of systematic reviews published in *Effective Care in Pregnancy and Childbirth* (Chalmers 1989). The database became a regularly updated electronic publication in 1989, developed into *Cochrane Pregnancy and Childbirth Database* in early 1993, and formed the basis of the broader *Cochrane Database of Systematic Reviews (CDSR)*, launched in 1995. Work on a handbook to support authors of Cochrane Reviews had begun in 1993, and the first version was published in May 1994. Over its first 20 years, Cochrane has grown from an initial group of 77 people from nine countries who met at the first Cochrane Colloquium in Oxford in 1993 to over 31,000 contributors from more than 120 countries in 2015, making it the largest organization involved in this kind of work (Allen 2006; Allen 2007; Allen 2011). Cochrane is now an internationally renowned initiative (Clarke 2005; Green 2005).

1.1.3 Cochrane organization and structure

Cochrane currently involves over fifty Cochrane Review Groups (CRGs), responsible for supporting the production and publication of reviews within specific areas of health. The review authors working with these groups include researchers, health professionals and people using healthcare services (consumers), all of whom share a common enthusiasm for generating reliable, up-to-date evidence relevant to the prevention and treatment of specific health problems or groups of problems.

CRGs are supported in this work by Methods Groups, Centres, Fields and by the Cochrane Editorial Unit (CEU). Cochrane Methods Groups provide a forum for methodologists to discuss development, evaluation and application of methods used to conduct Cochrane Reviews. They play a major role in the production of the Cochrane Handbook for Systematic Reviews of Interventions and, where appropriate, chapters in this volume contain information about relevant Methods Groups. Members of these Methods Groups have made major contributions to systematic review methodology (Chandler 2013). Cochrane Centres are located in different countries. Collectively, they represent all regions of the world and provide training and support for review authors and CRGs in addition to advocacy and promotion of access to Cochrane Reviews. Cochrane Fields focus on broad dimensions of health, such as the setting of care (e.g. primary care), the type of consumer (e.g. children), or the type of intervention (e.g. vaccines). People associated with Fields help to ensure that priorities and perspectives in their sphere of interest reflect the work of CRGs. The CEU provides strategic support and direction, and leads initiatives to improve and assure the quality of review activity across Cochrane.

1.2 Systematic reviews

1.2.1 The need for systematic reviews

Healthcare providers, consumers, researchers, and policy makers are inundated with unmanageable amounts of information, including evidence from health research. It is unlikely that they will have the time, skills and resources to find, appraise and interpret all this evidence and to incorporate it into healthcare decisions. Cochrane Reviews respond to this challenge by identifying, appraising and synthesizing research-based evidence and presenting it in an accessible format (Mulrow 1994). The requirement for systematic reviews to appraise the ever-growing proliferation of individual research studies has, if anything, become more important in recent years (Mallett 2003; Bastian 2010).

1.2.2 What is a systematic review?

A systematic review attempts to collate all empirical evidence that fits pre-specified eligibility criteria in order to answer a specific research question. It uses explicit, systematic methods that are selected with a view to minimizing bias, thus providing more reliable findings from which conclusions can be drawn and decisions made (Antman 1992; Oxman 1993). The key characteristics of a systematic review are:

- a clearly stated set of objectives with pre-defined eligibility criteria for studies;
- an explicit, reproducible methodology;
- a systematic search that attempts to identify all studies that meet the eligibility criteria;
- an assessment of the validity of the findings of the included studies, for example through the assessment of risk of bias; and
- a systematic presentation, and synthesis, of the characteristics and findings of the included studies.

Many systematic reviews contain meta-analyses. Meta-analysis is the use of statistical methods to summarize the results of independent studies (Glass 1976). By combining information from all relevant studies, meta-analyses can provide more precise estimates of the effects of health care than those derived from the individual studies included within a review (see Chapter 9, Section 9.1.3). Meta-analyses facilitate investigations of the consistency of evidence across studies, and the exploration of differences across studies.

1.3 Cochrane Reviews

Cochrane has developed a rigorous approach to the preparation of systematic reviews, with a structured review model. Cochrane publishes four main types of systematic reviews, summarized in Sections 1.3.1 to 1.3.4 and has a programme to explore development of review methods for other types of research question.

1.3.1 Reviews of the effects of interventions

Most Cochrane Reviews consider evidence on the effects of health or healthcare interventions. These reviews focus primarily on randomized studies as the most robust research design for assessment of the effects of interventions. Where evidence is unlikely to be found in randomized studies, for example for many adverse effects of interventions, or for large-scale interventions such as in public health or organizational change, reviews include non-randomized studies. Intervention reviews may additionally address broader issues such as economic issues or patient experiences of the intervention.

Cochrane has recently developed quality standards for the conduct and reporting of reviews. These standards summarize attributes for the conduct, and reporting, of reviews of interventions as set out in this *Handbook* (see Chapter 2, Section 2.4).

1.3.2 Reviews of diagnostic test accuracy

Cochrane has published systematic reviews of diagnostic test accuracy (DTA) in CDSR since 2008 (Leeflang 2013). These reviews evaluate how correctly a test detects the presence or absence of a target condition. Cochrane DTA reviews cover target conditions across health, including both pathologically defined diseases and more loosely defined indications for which treatments may be available. All types of tests are eligible, including: signs and symptoms from the patient history and examination; questionnaire-based tools, scores and decision rules; laboratory tests including biochemical, immunological, genetic, genomic and other 'pan-omic' technologies; imaging tests; and physiological measurements. Evaluation of the accuracy of a test is one component of the assessment of whether test use could lead to improvement in patient outcomes. Direct evaluation of how a test (and consequent decision-making and interventions) actually affect patient outcomes is best assessed by randomized studies that

incorporate the effects of interventions that follow the test result. Such studies fit within the structure of Cochrane Intervention Reviews. However, randomized studies of test use are rare (especially outside the context of screening; Ferrante di Ruffano 2012), whereas accuracy studies are relatively common and provide most of the available evidence to guide test use, which makes them worthy of detailed systematic review. Although the stages in a DTA review are the same as for reviews of interventions, specific methodological challenges are encountered at each step: from formulation of review questions, through searching for and locating studies, assessing study quality, meta-analysis and interpretation of findings. Full methodological details are described in a separate Cochrane Handbook for Diagnostic Test Accuracy Reviews (http://srdta.cochrane.org/handbook-dta-reviews).

1.3.3 Overviews of Reviews

Cochrane Overviews of Reviews (Overviews) compile evidence from multiple systematic reviews into a single accessible and usable document. They are intended primarily to synthesize multiple Cochrane Reviews addressing a set of related interventions, populations, outcomes, or conditions, although other published non-Cochrane reviews may also be included. Cochrane Overviews provide the reader with a quick and comprehensive guide to reviews relevant to a specific decision. Overviews are aimed at decision makers, such as clinicians, policy makers, or informed consumers, who are accessing the CDSR for evidence on a specific problem. Overviews of Reviews on the effects of interventions are addressed in detail in Chapter 22 (see Section 22.1).

An overview of systematic reviews of diagnostic test accuracy (DTA Overview) can be used to synthesize and compare findings from a related set of test accuracy reviews. For example, an overview might bring together and compare the findings of separate reviews of alternative tests used to diagnose the same condition at the same point in the patient pathway. DTA Overviews also have a role in evaluating the accuracy of tests for the detection of closely related target conditions (particularly when they form part of a set of differential diagnoses), and in evaluating the performance of the same test across different settings. DTA Overviews are best planned when commencing on a portfolio of related individual systematic reviews, and plans for incorporation in a DTA Overview should be mentioned in the protocols of the individual reviews.

1.3.4 Reviews of methodology

Cochrane Methodology Reviews seek to answer questions about various aspects of the methods for systematic reviews, randomized studies and other evaluations of health and social care. They provide an evidence base for the methods of these evaluations, as well as providing descriptive accounts of other relevant issues, for example, to show the scale of problems faced by researchers working on systematic reviews or making decisions about health and social care. Cochrane Methodology Reviews use the widest range of study designs of Cochrane Reviews, including:

- experimental studies such as randomized studies to compare different strategies to increase response rates to surveys;
- comparative observational studies to examine the relationship between the use of reporting guidelines and the quality of research reports; and
- · descriptive observational studies of the proportion of studies presented at conferences that are also published in full.

Cochrane Methodology Reviews have a particular structure, based on the structure of Cochrane Intervention Reviews but with changes to some of the headings and sub-headings. The Cochrane Methodology Review Group has editorial responsibility for all Methodology Reviews. Appendix A provides a guide to the contents of a Cochrane Methodology protocol and review.

1.4 Publication of Cochrane Reviews

1.4.1 The Cochrane Library

Cochrane Reviews are published in full online in the *CDSR*, which is a core component of the Cochrane Library (www.thecochranelibrary.com). The Cochrane Library was first published in 1996, and is now an online collection of six databases (listed in 1.4.a) published by Wiley-Blackwell. In addition to the *CDSR*, the Cochrane Library includes additional resources that are provided by the Centre for Reviews and Dissemination (CRD) in York, UK. It is available free at the point of use in some countries, thanks to national licences and free one-click access provided by Wiley-Blackwell and Cochrane in most low- and middle-income countries, in association with Evidence Aid. Elsewhere it is subscription based, or pay-per-view. Since February 2013, reviews that have been published in full, or updated in full for the first time, now become freely available to all 12 months after their initial publication under an open access model.

Box 1.4.a: Databases published in the Cochrane Library

Active databases

The CDSR contains the full text (including methods, results and conclusions) for Cochrane Reviews and protocols.

The Cochrane Central Register of Controlled Trials (CENTRAL) is a highly concentrated source of reports of randomized and quasi-randomized studies. The majority of CENTRAL records are taken from bibliographic databases (mainly MEDLINE and Embase), but records are also derived from other published and unpublished sources.

The Health Technology Assessment database contains details of completed and ongoing health technology assessments (studies of the medical, social, ethical, and economic implications of healthcare interventions). It is produced by CRD, using information obtained from members of International Network of Agencies for Health Technology Assessment (INAHTA) and other health technology assessment organizations.

Archived databases

The Database of Abstracts of Reviews of Effects (DARE), assembled and previously maintained by CRD, contains critical assessments and structured abstracts of other systematic reviews, conforming to explicit quality criteria. This database was archived in March 2015.

The Cochrane Methodology Register (CMR) contains bibliographic information on articles and books on the science of reviewing research, and a prospective register of methodological studies. This database was archived in July 2012.

NHS Economic Evaluation Database (EED) contains appraised economic evaluations highlighting their relative strengths and weaknesses. It was produced by CRD. This database was archived in March 2015.

1.5 Handbook structure

There are three parts to the Handbook. Part 1 provides general information on Cochrane, its principles and the specific structure of Cochrane Reviews, their preparation, reporting, publication and maintenance. Part 2 provides the requisite methods to conduct a review with the required minimum standards. Part 3 covers a range of special topics for consideration when undertaking a Cochrane Review.

1.6 Chapter information

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