# FIT FOR THE CHALLENGE:
## THE NEW COCHRANE HANDBOOK

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### Shifting sands

The last 25 years in health have been notable for the emergence of evidence synthesis and its role in making sense of exploding global research output. By any measure, systematic reviews are a major feature of the research landscape, helped in part by their versatility and capacity for reinvention. Review labels continue to proliferate, expanding what is both conceivable and feasible to produce. Historically, what was mostly a binary choice between traditional reviews and systematic reviews is now a smorgasbord that encompasses reviews variously described as scoping, mapping, narrative, umbrella, mini, living, rapid and even ultra-rapid. You are not just imagining this burgeoning array of review types - a recent study identified 48 types, categorised into seven families (Sutton et al., 2019). Although fragmentation and specialisation of reviews may create definitional confusion, it is also a sign of a dynamic research area that is continually exploring ways of developing knowledge outputs to meet the diverse needs of decision-makers.

Twenty-five years ago, when Cochrane started, the majority of systematic reviews published globally were probably Cochrane reviews, and Cochrane's methods became *the* methods to follow. Inevitably, as systematic reviews became more accepted as valid research outputs and the methods more widely disseminated, the number being conducted and published grew dramatically. Fast forward to today and the number of reviews is staggering. There are close to 25,000 published annually in PubMed and there has been a three-fold increase in reviews registered in PROSPERO since 2015 - from 5000 to nearly 15 000 annually. At one level this reflects the widespread acceptance of the role of systematic reviews in informing decisions (e.g. in guidelines), however, their

ubiquity is potentially problematic, with criticisms of unnecessary duplication leading to research waste (Ioannidis, 2016).

Many universities encourage involvement in systematic reviews as a practical way to learn valuable research skills, and they are often a more attractive proposition for students than pursuing primary research projects. But as research synthesis has evolved into its own distinctive area of scientific research, so too has its specialisation - we can see this in the methodological and technical advances, and the competencies required by author teams to produce high-quality reviews. So, where does this leave the humble reviewer embarking on their first review? What can Cochrane offer to those involved in writing and supporting systematic reviews?

## There is no shortage of guidance

There are many manuals, guidelines, handbooks and all manner of online resources and materials that would-be reviewers can choose from to help navigate the review process. Further, many university library websites have extensive teaching and learning resources dedicated to supporting staff and students undertake systematic reviews. A long-standing and essential resource is the Cochrane Handbook.
The new edition of the *Cochrane Handbook for Systematic Reviews of Interventions* was published in October 2019 and is available free online at training.cochrane.org/handbook or in hard copy (Higgins et al., 2019). This second print edition comes in at just shy of 700 pages, putting it firmly in the super-heavyweight division, and brings together the expertise of over 100 contributing methodologists. As the first major revision in a decade, the new Handbook reflects the technical developments in evidence-based methods that have occurred over that time and represents Cochrane's current consensus, backed by methodological research, on the most appropriate methods for systematic reviews of interventions (Cumpston et al., 2019).

The printed Handbook has three parts. (There is an online-only section, specific to authors working with Cochrane, that includes a useful chapter on reporting the review.) Part 1 covers the core methods for conducting intervention reviews of randomised trials and divides the review process into 15 steps, with a chapter devoted to each. Parts 2 and 3 focus on specific perspectives in reviews (e.g. equity, adverse effects, qualitative evidence) and other topics (e.g. inclusion and assessment of non-randomised evidence).

## What's new?

Cochrane has always strived to produce reviews that are both valid as well as useful to decision-makers but has sometimes struggled to achieve the optimal balance. Many of the advances in methods in recent years concern reviews that address complex questions of multi-component interventions, health systems and public health - challenging reviews that Cochrane has increasingly taken on because they respond to the needs of end users. The new areas of guidance in the Handbook speak to the broad scope of Cochrane reviews and may help lay to rest the long-held perception that Cochrane is all about narrowly defined meta-analyses of randomised trials.
Investigating bias is a favourite pastime of methodologists and new or updated **guidance on bias** features in several chapters: version 2 of the Cochrane risk of bias tool for randomised trials; ROBINS-I tool for assessing the risk of bias in non-randomised studies; and risk of bias due to missing results. Another development is the incorporation of **network meta-analysis** as a core method. This is where multiple treatments (e.g. SSRIs for depression) are compared directly (in head-to-head comparisons) and indirectly (within a network of trials), enabling reviewers to generate a league table of treatment effectiveness. Complexity in reviews, and the problems caused by data deluge in some primary studies, has been tackled through new guidance that urges authors to stipulate their planned syntheses upfront. Linked to this is new guidance on **synthesising results** across studies (using different types of plots and graphs) when meta-analysis is not feasible.

## Searching for studies

The searching chapter has been extensively revised and expanded to include the step of selecting studies. It is notable that among the technical specialists who are involved in reviews, the role and value of librarians and information specialists remains widely recognised, in part because the validity of systematic reviews depends on objective, thorough and reproducible searches (Metzendorf & Featherstone, 2018).
The days of relying on a single report or publication, retrieved from a bibliographic database, as the sole source of evidence about a study are disappearing. Studies have lifecycles and continually 'shed' data and information that can be critical to the reliability of the evidence synthesis. (We are seeing this play out in the coronavirus pandemic, where studies and their associated reports (register entries, protocols, preprints, etc.) are being forensically scrutinised (Armstrong, 2020).) Thus, in addition to bibliographic databases, the chapter section on **sources to search** includes information about ongoing studies, unpublished data sources, trials results registers, regulatory agency sources and clinical study reports. Empirical studies inform the advice in the Handbook so, for example, there is a discussion of the pros and cons of searching multiple databases and when it might be appropriate to deviate from standard practice.

The section on designing **search strategies** deals with all the routine issues (controlled vocabulary, text words, Boolean, limits, filters, etc.) as they apply to systematic reviews, plus there is a discussion of peer review of search strategies, use of alerts, identifying fraudulent and retracted publications, and when to stop searching. The short section on **documenting and reporting the search** process covers the 'what, when and how' and ties in with requirements of PRISMA.
In addition to the content covered in the chapter, there is a comprehensive **online technical supplement** that gives more detail about each type of information source, including advice on how to access and search them, and consideration of the value they bring. Linked to the technical supplement is a regularly updated spreadsheet that gives the URL for each resource by category.

## Selecting studies

Screening records can be enormously resource intensive and is why the time taken to complete a full systematic review can blow out to more than two years (Borah et al., 2017). A lot depends on technology to help ease this and other bottlenecks in the review process, such as bias assessment and data extraction. But while many tools and applications are available (see SR Toolbox) their uptake has been mixed, with concerns expressed about workflow compatibility, user experience and licensing (van Altena et al., 2018). Even when automation tools can be integrated into workflows, it's interesting to quantify the efficiency gains that are attributable to tech and automation as opposed to the organisation of human effort (Clark et al., 2020).
Leaving these debates to one side, the Handbook covers some of the common approaches to facilitate more efficient study selection. These include systematic review management tools (e.g. Covidence) and the use of machine learning algorithms to support screening prioritisation (where the machine continually reorders the sequence of unscreened records based on their relevance). The most significant innovation for Cochrane has been the creation of machine learning classifiers to speed up the process of identifying randomised trials from several sources, including PubMed, Embase, CINAHL and ClinicalTrials.gov. Because of the vast amounts of training data generated by Cochrane Crowd, these classifiers can very accurately determine the likelihood that a record reports a randomised trial. Cochrane is now routinely employing machine classifiers centrally (via its evidence pipeline) to efficiently harvest all randomised trials which are then fed directly into Cochrane's trials register in the Cochrane Library (Marshall et al., 2018) (Thomas et al., 2019).

## Training and support

A new feature of the Handbook (both print and online) is the integration with the *Methodological Expectations of Cochrane Intervention Reviews* (known as the MECIR Standards); these are the mandatory or highly desirable methodological standards to which all Cochrane reviews are expected to adhere and cover both conduct and reporting (Higgins et al., 2020). Each standard comprises a concise instruction (e.g. to

search trials registers and repositories of results) pus a rationale. The 75 standards, 21 of which cover searching and selecting studies, are the distillation of the Handbook to its bare essentials.

Those looking to complement the Handbook with other resources should check out Cochrane Training (training.cochrane.org). In addition to the 11 interactive online learning modules, there is an extensive collection of recorded webinars presented by the methodologists responsible for developing the guidance and writing the Handbook chapters.

One other major development in systematic reviews to look out for is the new PRISMA Statement (Preferred Reporting Items for Systematic Reviews and Meta-Analyses). The original PRISMA (Moher et al., 2009) has been extensively updated over the last two years and is expected to be published later in 2020. In the meantime, the recently-completed PRISMA-Search Extension (Rethlefsen et al., 2020) covers all of the essentials for reporting the search.

Finally, a challenge facing readers of systematic reviews is understanding how their conduct might affect their trustworthiness. As a group that is actively involved in supporting many systematic reviews, health librarians and information specialists have a role in promoting best practice, particularly when it comes to searching. Our hope is that the guidance and advice in the new Cochrane Handbook, which has been written by information specialists, will prove an invaluable source of reference.

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