COVID-END
COVID-19 Evidence Network to support Decision-making

Resources and tools for researchers considering and conducting COVID-19 evidence syntheses

Prepared by the COVID-END Synthesizing Working Group

1. Value of evidence synthesis to inform decision making

The COVID-19 pandemic has led to an explosion of activities among all types of researchers, including in the evidence-synthesis, technology assessment and guideline-development communities. COVID-END has prepared tips for individual researchers and research teams who are involved or who want to become involved in preparing timely, relevant and high-quality evidence syntheses, technology assessments and guidelines to support decision-making about COVID-19.

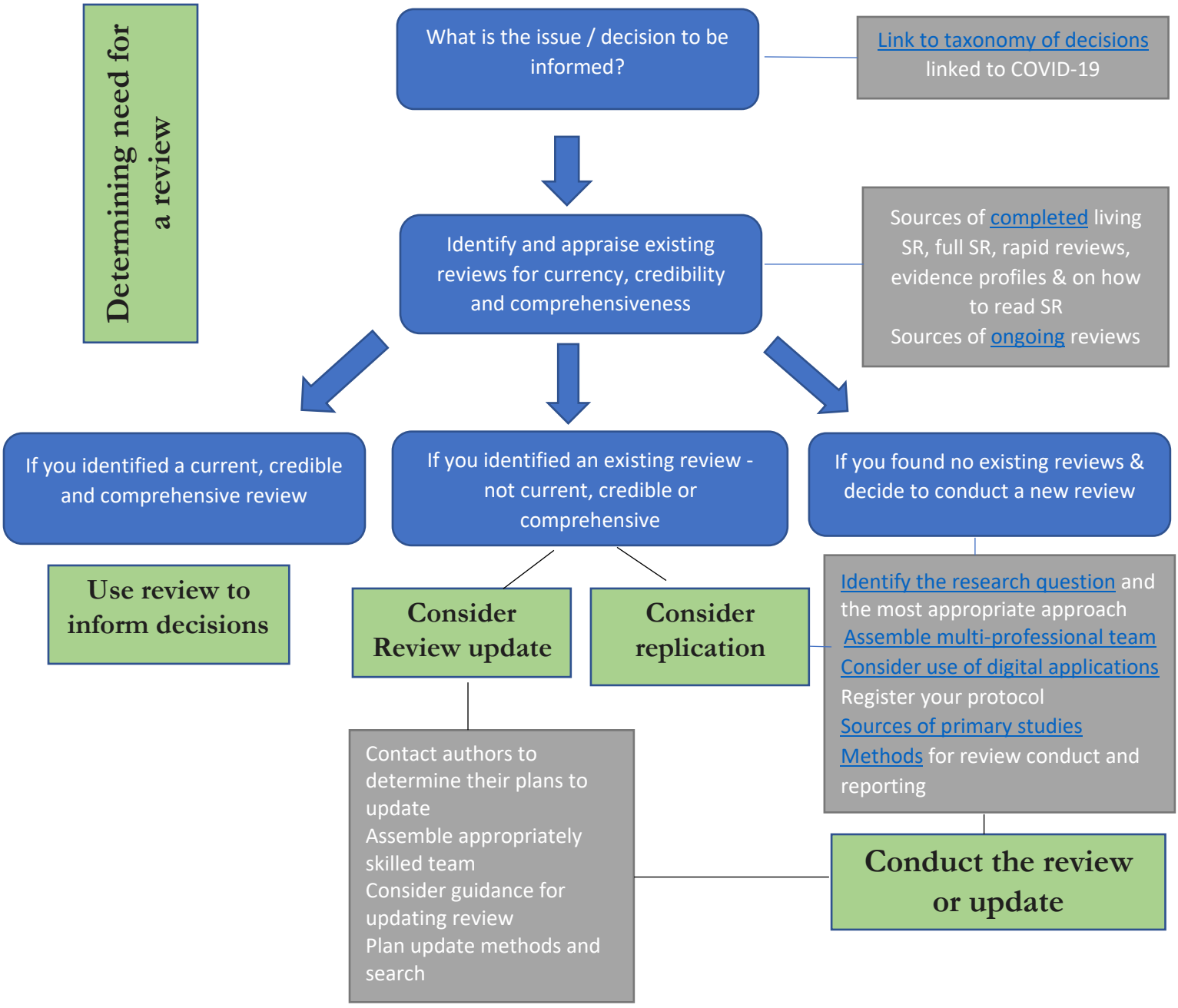
There are many different types of evidence synthesis and this toolkit on COVID-19 evidence synthesis focuses on – rapid reviews, scoping reviews, systematic reviews (SR), and living SR. the table below provides some key definitions which assist in distinguishing between various types of synthesis.

> Akl, E. A., Haddaway, N. R., Rada, G. and Lotfi, T. (2020). Evidence synthesis 2.0: When systematic, scoping, rapid, living, and overviews of reviews come together. Journal of Clinical Epidemiology. https://doi.org/10.1016/j.jclinepi.2020.01.025
>
> Gough D, Thomas, J., & Oliver, S. (2019). Clarifying differences between reviews within evidence ecosystems. *Systematic Reviews, 8 (1)*, 170. doi:10.1186/s13643-019-1089-2 https://systematicreviewsjournal.biomedcentral.com/articles/10.1186/s13643-019-1089-2

Type of evidence synthesis	Definition
Inventories	Inventories only list the evidence that is available on a given topic. There is no attempt to appraise, summarize or synthesize the evidence for further use, nor is there an attempt to present conclusions or recommendations to the knowledge user.
Non systematic scoping review of the literature	Non systematic scoping reviews undertaken with the objective of providing a preliminary assessment of potential size and scope of available research literature.
Systematic scoping review / Systematic maps of the literature	A systematic scoping review / Systematic map describes what has and not been studied about a research question. It uses systematic reproducible and transparent methods to identify, code and report this literature.
Systematic review	A systematic review aims to answer a clearly formulated research question using the findings of already completed research. It uses systematic,reproducible and transparent methods to identify, select and appraise the relevant studies , and analyse their findings. It can address different types of questions – effects of prevention or treatment strategies, diagnostic test accuracy, prognosis, risk factors, etc. Depending on the question they may utilise different forms of evidence, including qualitative data and may evaluate simple and complex interventions.

Rapid response briefs	Rapid response briefs present a summary of the best available evidence in a synthesized and contextualized manner, in direct response to a decision-maker's question. They are knowledge translation products created through formal methods to synthesize and appraise the evidence. They do not generate new knowledge but use findings that are already available, especially from existing systematic reviews.
Rapid reviews	A rapid review accelerates the process of conducting a systematic review through streamlining or omitting specific methods to produce evidence for stakeholders in a timely manner. It is increasingly feasible to conduct a systematic review rapidly utilising technology advancements or crowd-sourcing but the term rapid review is usually used when there is some compromise in scope or rigour of method of the review (which may limit the evidence claims that can be made). Rapid reviews aim to be systematic but may be limited in scope or rigour of method which may limit the evidence claims that can be made from them.
Living systematic review	A living systematic review is a review that is continually updated, incorporating relevant new evidence as it becomes available. Living reviews have become possible with the use of information technology to provide automated searching for newly published studies. In the context of the COVID-19 pandemic designating a systematic reviews as 'living' may indicate that the researchers a) anticipate that new evidence is likely to emerge that will influence the results of the review, and b) that they aim to incorporate such new data as it become available ('in real time') "Living" attributes can also be applied to other forms of evidence synthesis.
Methods and Multi-component reviews	Mixed methods review include a number of different forms of research evidence (such as for example quantitative and qualitative studies) in the review. In some cases these different forms of evidence are considered together. In other cases, the review question is ivided into subquestions that are addressed in different sub-components of the review.

This flow diagram highlight key steps (blue blocks) in the overarching process (in green) with proposed tools to link to in grey. These are unpacked further from page 5 onwards.



2. Determining the need for a review

2.1 What is the issue / decision to be informed?

You may get ideas for an evidence synthesis or technology assessment by reviewing the four-part taxonomy of decisions that will need to be informed by research evidence as the pandemic and pandemic response enter (or re-enter) different phases. It is useful to engage with and involve key stakeholders in order to clarify the research question.

2.2 Avoiding duplication of effort – look for existing and ongoing evidence synthesis

In the current context, it is more important than ever to avoid unnecessary duplication of effort. This represents research waste. You can address this by seeking to identify existing published review syntheses and those in preparation.

2.2.1 Access and assess existing evidence syntheses

Identify existing evidence syntheses

Identifying the reviews and evidence syntheses that already exist is an essential first step to avoid duplication of effort and research waste. COVID-END has identified many of the most important searchable databases that already include published systematic reviews. If you are working directly with policy and decision-makers, it may be helpful to point to work that has already been reviewed that they can consider for their own context.

Databases with access to variety of reviews across specific organisations

- COVID-19+ by McMaster PLUS (includes critically appraised systematic reviews and single studies organized by quality level and document type)
- Evidence Aid - Summaries of systematic reviews that may be relevant to COVID-19 in eight broad areas (infection prevention and control; clinical characterization and management; therapeutics and vaccines; public-health interventions; health systems and services; epidemiology; ethical considerations; and social science in response).
- L*VE by Epistemonikos (includes existing systematic reviews of effects and the primary studies, including trials, that were included in the reviews)
- LitCovid from PubMed (includes systematic reviews and single studies organized by mechanism, transmission, treatment, case report, and epidemic forecasting)
- TRIP database (includes systematic reviews and single studies organized by document type)
- U.S. Veterans' Affairs (VA) Evidence Synthesis Program - Inventory of living (and regular) systematic reviews and 'rapid reviews' (completed and in progress), with a flag for living reviews and for reviews meeting minimum quality standards

Full systematic reviews (and derivative products) from specific organisations

- AHRQ EPC Program - https://effectivehealthcare.ahrq.gov/products/covid-resources/overview
- Cochrane - Special collections of Cochrane systematic reviews relevant for COVID-19 and Prioritized Cochrane systematic review updates (same page as above but lower down the page; the rapid reviews are listed in the relevant section below). Cochrane Reviews address questions that are relevant to health care and its delivery.
- Campbell Collaboration - Blog profiling Campbell reviews that are relevant to COVID-19. Campbell Reviews cover areas such as social welfare, crime, international development and education amongst others
- JBI - https://jbi.global/ebp/covid-19 includes JBI Evidence Summaries that provide a summary of the best available evidence related to a clinical topic including best practice recommendations to help clinicians mobilise evidence into practice, and JBI Recommended Practices that provide standardised, detailed descriptions of best practice care procedures.

Other useful sources of synthesized data

- DistillerSR (includes curated, tagged and downloadable references to single studies)
- Health Systems Evidence and Social Systems Evidence – *Coming soon* - Systematic reviews and economic evaluations about health- and social-system arrangements presented with their focus on or relevance to COVID-19, quality rating, recency of search, and countries where the research was conducted
- SRDR (https://srdr.ahrq.gov/) (includes underlying data from individual studies included in a systematic review)
- McMaster Optimal Aging Portal - Citizen-targeted summaries of systematic reviews that may be relevant to staying active and engaged while practicing physical distancing
- Literature Review (includes manually identified systematic reviews and single studies organized by topic and medical specialty

Grading of Recommendations, Assessment, Development and Evaluations (GRADE) evidence profiles

Some guidelines bodies and decision makers favour the efficient production of GRADE evidence profiles rather that the systematic review reports. GRADE evidence profiles describe the results of a given review, focussing on the main outcomes of interest for a given comparison of interventions. They report the direction and magnitude of any effect and the degree of certainty that an effect estimate reflect the true effect, using pre-determined criteria.

COVID-NMA: includes full evidence profiles for all comparisons of pharmaceutical, non-pharmaceutical treatments, preventive and rehabilitation interventions.
L*OVE Epistemonikos: includes interactive Summary of Findings Tables for its new Living Evidence Syntheses

Appraising existing evidence syntheses

There are a number of resources that can be used to evaluate the credibility of published reviews or evidence syntheses. Rohwer et al provides a short guide on finding, reading and interpreting systematic reviews, as well as applying the results.

Rohwer A et al. Reading systematic reviews to answer clinical questions. Clinical Epidemiology and Global Health. 2014; 2:39-46

AMSTAR 2 tool:
A critical appraisal tool for systematic reviews that include randomised and/or non randomised studies of healthcare interventions

Article
Tool
Guidance

ROBIS tool:
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4687950/

National Collaborating Centre for Methods and Tools (NCCMT) Quality Assessment Tool: This includes a one page assessment checklist followed by a 'Quality Assessment Tool Dictionary' that provides guidance on how to answer each question. https://healthevidence.org/documents/our-appraisal-tools/quality-assessment-tool-dictionary-en.pdf

2.2.2 Identify ongoing evidence synthesis

Similarly, it is important to identify reviews that are already in the pipeline, and this can also be done by searching for review titles.

- PROSPERO database for health care related reviews
- National Collaborating Centre for Methods and Tools for rapid reviews
- International Platform of Registered Systematic Reviews and Meta-Analysis Protocols (users can search for free, but registering requires payment) https://inplasy.com
- Centre for Evidence Based Medicine (CEBM): Rapid Reviews as part of Oxford COVID-19 Evidence Service: Current questions under review
- Evidence Synthesis Program COVID-19 Evidence Reviews (Unpublished)

Where credible, current and comprehensive reviews exist, these may be sufficient to address the question that you were proposing to research. In some cases, as the Figure demonstrates, the reviews will not be current. In such cases an update may represent a more useful and efficient contribution to the research literature than a review that starts from scratch (See Section 3 for further details on updating evidence synthesis).

Sometimes, having identified and assessed the existing research and that in preparation, researchers may decide that for a variety of reasons the review should be replicated. This may relate to the formulation of the question, the context, or uncertainties around the credibility of conduct or reporting. Conscious replication of reviews in such instances is fully justifiable (See Section 4 for further details on conducting evidence synthesis).

3. Updating out of date reviews

Where you identify reviews that appear out of date, contacting the original author team is useful to determine whether they have plans to undertake an update. Depending on the circumstances, it might be appropriate to either await a planned update, provide support to the existing team, or to create a new team to update the review separately.

Updating an existing review is generally more efficient than starting from scratch with a new review. The decision to update may be influenced by a range of factors such as the likelihood that new research may influence the result or have the potential for impact on health, the degree of certainty of the findings of the existing review, the methods applied, and any awareness you have of other important factors that may not have been sufficiently considered by the original team. Updates may be complete or partial, for example, focusing only on specific PICO characteristics, or may amend the types of studies that are identified and included such as searching for non randomised studies to identify serious harms.

Guidance and a checklist to guide the decision on when and how to update a systematic review can be found here. (Garner P, Hopewell S, Chandler J, MacLehose H, Akl E A, Beyene J et al. When and how to update systematic reviews: consensus and checklist *BMJ* 2016; 354 :i3507)

4. Conducting new evidence synthesis

If you cannot find a current, credible and comprehensive evidence synthesis, or you have a rationale for replicating an existing evidence synthesis, follow this guidance to ensure a robust product.

4.1 Identifying the research question and the most appropriate approach

Systematic reviews and evidence syntheses come in many forms and the preferred methodological approach varies accordingly. Identifying the question accurately is sometimes straightforward, but in most cases a thoughtful discussion and assessment of the context, concepts and challenges are always beneficial. Exploration and engagement with those interested in the results of the review will improve the quality and utility of the output. This may include funders of the review, policy makers, professional practitioners, users of relevant services, and other stakeholders.

4.1.1 Developing a review question

General resources for developing a review question:

- Developing a Research Question
  A research guide produced by the University of Maryland
- Research question frameworks
  A research guide produced by the Welch Medical Library, Johns Hopkins University

Organisations that are publishing lists of high priority questions on which they are seeking researchers include:

- Cochrane
  https://covidrapidreviews.cochrane.org/search/site

4.1.2 Determine type of evidence synthesis

The following resource and research article aim to guide researchers in determining the appropriate methods for their review:

- **What review is right for you?**
  This is an algorithm developed by the Knowledge Translation Program of the Li Ka Shing Knowledge Institute, St. Michael's Hospital, Toronto, Canada
- **What kind of review should I conduct?**
  Munn, Z., Stern, C., Aromataris, E. *et al.* What kind of systematic review should I conduct? A proposed typology and guidance for systematic reviewers in the medical and health sciences. *BMC Med Res Methodol* **18,** 5 (2018). https://doi.org/10.1186/s12874-017-0468-4

4.2 Considering how the review is most likely to have a positive impact on decision making

Engaging with those decison makers who are most likely to be influenced by the review is valuable in guiding decisions about how the review is conducted and reported. Where possible, this should form part of the preparation work so that it can inform the subsequent review from the outset. Such engagement may inform critical elements of the review's conception, lead to co-production of the review with key stakeholders, and may influence decisions about the packaging of the completed review designed to register maximum impact.

4.3 Assembling an appropriate team

If you are not already an individual or group with rich experience in synthesizing research evidence or in preparing technology assessments for decision-makers, consider working with others who have such experience. Similarly, if you are not already an individual or group working in close partnership with decision-makers, consider working with groups that have such partnerships (and if you don't have access to such a group, check out our tips for supporting decision-makers. A complete systematic review team generally includes or has access to individuals who have information retrieval, content, statistical and broader methodological skills. Involving individuals with relevant content expertise is also highly desirable in most cases. Of course, any one individual may bring more than one of these attributes, but conducting high quality systematic reviews require a team approach.

4.4 Use of digital applications and crowd to accelerate review production

Review support: The following tools aim to provide support for systematic reviewers, usually through aiding the study identification and data extraction processes.

Tool	Link	Description
Covidence	https://www.covidence.org/home	**Covidence** is a systematic reviews production tool for title/abstract screening, full-text screening, data abstraction, and quality assessment.
Distiller SR	https://www.evidencepartners.com/products/distillersr-systematic-review-software/	It allows users to collaborate in real-time by accessing and extracting data from the web. **Distiller SR** also allows users to create custom forms, reports and metric trackers.
Epistemonikos / LOVE tool	https://www.epistemonikos.cl/proyectos/love/	Maps, organizes evidence
EPPI-Reviewer	https://eppi.ioe.ac.uk/EPPIReviewer-Web	**EPPI-Reviewer** is an online software application which supports authors and editors in writing all types of systematic reviews, particularly in complex areas including meta-analysis, framework synthesis, and thematic synthesis
JBI SUMARI	https://www.jbisumari.org/	JBI SUMARI supports 10 review types and facilitates the entire review process, from protocol development, team management, study selection, critical appraisal, data extraction, data synthesis and writing your systematic review report in one easy to use web application
ReviewManager	https://training.cochrane.org/online-learning/core-software-cochrane-reviews/revman	**RevMan** Web is the online platform recommended for Cochrane intervention reviews. **RevMan** Web has been designed to integrate with other systematic review software and new features and updates are added regularly
SRDR	srdr.ahrq.gov	SRDR is a database of systematic reviews and the individual data abstraction tables that go into production of the review. These evidence tables are available for download and reuse under the creative commons license.

Automation tools: The following aim to utilize data mining and automated approaches to facilitate the review process.

Tool	Link	Description
Epistemonikos / LOVE tool	https://www.epistemonikos.cl/proyectos/love/	Maps, organizes evidence
EPPI-Reviewer	https://eppi.ioe.ac.uk/EPPIReviewer-Web	**EPPI-Reviewer** is an online software application which supports authors and editors in writing all types of systematic reviews, particularly in complex areas including meta-analysis, framework synthesis, and thematic synthesis
Rayyan	https://rayyan.qcri.org/	Speeds up the process of screening and selecting studies
RCT Classifier	https://community.cochrane.org/sites/default/files/uploads/QRG_RCT_classifier.pdf	Machine learning routine that helps to distinguish between reports of Randomised (and quasi-Randomised) Controlled Trials (RCTs) and non-RCTs.
Robotreviewer	https://www.robotreviewer.net/	Automatically extracts and synthesises data from Randomized Controlled Trials

Cochrane Crowd and Task Exchange: Cochrane Crowd is organising specific COVID related screening challenges designed to enable the community to come together each week. These generally focus on identifying RCTS. Cochrane Task Exchange has a specific area where people wishing either to commission or to conduct COVID related tasks can be matched.

4.5 Register your review protocol

In order to assist others, you should register your review protocol in the registries described above. You can do this in PROSPERO, or with an appropriate review group in Cochrane or the Campbell Collaboration (which provide quality assurance, publishing, translation and other benefits for eligible and accepted titles and protocols). The protocol should be prepared and published in advance of the conduct of the review, to reduce the risk of bias and to clarify plans (for example, identifying the main outcomes of interest). Protocols should be freely accessible to readers as a key quality measure. Cochrane Reviews protocols are open access and it is also possible to publish protocols in journals such as *Systematic Reviews* or on the Open Science Framework.

4.6 Sources of primary studies

We strongly recommend engaging with an information scientist in order to prepare an appropriate search strategy, unless a member of the research team has the required skills and expertise.

4.6.1 Sources of primary studies on COVID

- Cochrane COVID-19 Study Register (includes all study types relevant to Cochrane reviews)
- Cochrane-NMA (includes a list of RCTs, with risk of bias assessment, data extraction into forest plots and GRADE evidence profiles)
- COVID-19+ by McMaster PLUS (includes critically appraised systematic reviews and single studies organized by quality level and document type)
- COVID-evidence (includes planned, ongoing, and completed trials on any intervention to treat or prevent COVID-19)

- L*VE by Epistemonikos (includes existing systematic reviews of effects and the primary studies, including trials, that were included in the reviews)
- LitCovid from PubMed (includes systematic reviews and single studies organized by mechanism, transmission, treatment, case report, and epidemic forecasting)
- World Health Organization (includes single studies)

4.6.2 Living maps of COVID studies

- CAMARADES (human, animal, in vitro and in silico studies, with protocol available but living evidence map not yet publicly available)
- Campbell UK and Ireland (living evidence map of human studies organized by geographic location)
- COVID-NMA (living evidence map and living network meta-analysis; evidence profiles about drug treatments are listed in a previous section)
- EPPI Centre (living evidence map of human studies organized by 11 areas of focus)
- Norwegian Institute of Public Health (living evidence map of human, animal, in vitro and in silico studies organized by eight areas of focus, with additional details here)

4.6.3 General sources

- Cochrane register of studies
- DistillerSR (includes curated, tagged and downloadable references to single studies)
- TRIP database (includes systematic reviews and single studies organized by document type)
- Clinicaltrials.gov (includes U.S. federal government-funded trials)
- International Clinical Trials Registry Platform (includes clinical trials)
- Medline

4.7 Methods for conducting rapid reviews

In some cases, the decision around the type of study is determined by circumstances or the expectations of the funders or sponsor. This has led to a rapid rise of 'rapid reviews'. In determining the type of rapid review that is appropriate for the context and timeline, the McMaster Health Forum has developed a Rapid Response guidance framework.

Cochrane:

- Support for authors
- Interim guidance from the Cochrane Rapid Reviews Methods Group
- Cochrane Training

National Collaborating Centre for Methods and Tools, McMaster, Canada

- Rapid Review Guidebook

Alliance for Health Policy and Systems research:

- Chapter briefs and Full guide

4.8 Methods for conducting scoping reviews

JBI - Scoping Reviews. Joanna Briggs Institute Reviewer's Manual. Available from https://reviewersmanual.joannabriggs.org/

4.9 Methods for conducting systematic reviews

Cochrane
Cochrane's mission is to promote evidence-informed health decision-making by producing high-quality, relevant, accessible systematic reviews and other synthesized research evidence

- Cochrane Handbook for Systematic Reviews of Interventions
- Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy
- Methods Expectations for Cochrane Intervention Reviews (MECIR)

Campbell Collaboration:
The Campbell Collaboration is an international social science research network that produces high quality, open and policy relevant evidence syntheses, plain language summaries and policy briefs

- Campbell Polices and Guidance

Agency for Healthcare Research and Quality:

- Methods Guide for Effectiveness and Comparative Effectiveness Reviews

JBI:
JBI is an international research organisation that develops and delivers evidence based information, including systematic reviews, software, education and training designed to improve healthcare proactice and outcomes
JBI Reviewer's Manual

4.10 Methods for conducting living systematic reviews

In the context of COVID-19, there are many questions where the evidence base is expanding rapidly. Living systematic reviews aim to ensure that completed reviews do not rapidly become out of date.

Not all subjects or research question are appropriate for a living SR, and the speed of updating will inevitably vary to suit the context and research question. Living SRs generally represent questions that are judged to be likely to have an important impact on decisions, where the evidence base is unstable and moving quickly, and where conclusions are vulnerable to changing. In order to designate a systematic review as 'living' the following criteria are needed: active monitoring of the evidence, real time incorporation of new data, the ability to communicate the review status and make visible the new data that have been added. (https://community.cochrane.org/review-production/production-resources/living-systematic-reviews#what). Living systematic reviews characteristically make use of digital technology or crowd-sourcing to support the process.

4.11 Guidance for reporting of the review

PRISMA guidelines (Preferred Reporting Items for Systematic Reviews and Meta-Analyses), and extensions apply to the following:

- PRISMA-P: Reporting of Protocols

- PRISMA-A: Reporting of Abstracts
- PRISMA-DTA: Reporting of reviews of Diagnostic Test Accuracy
- PRISMA-ScR: Reporting of Scoping Reviews
- PRISMA-CI: Reporting of Complex Interventions
- PRISMA-E: Reporting of Equity issues
- PRISMA-Harms: Reporting of Harms
- PRISMA-IPD: Reporting of SRs and meta-analyses of individual participant data
- PRISMA-NMA: Reporting of Network Meta-Analyses

Once published, notify groups listed in 2.2.1 of the completed review and consider uploading data into a data registry such as Figshare or SRDR to facilitate reuse of data.

For any comments or to suggest further resources to consider adding, contact
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