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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 focuses on – rapid reviews, scoping reviews, systematic reviews (SR), and living SR.

<table>
<thead>
<tr>
<th>Type of evidence synthesis</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rapid review</td>
<td>“A rapid review is a form of knowledge synthesis that accelerates the process of conducting a traditional systematic review through streamlining or omitting specific methods to produce evidence for stakeholders in a resource-efficient manner.” (C Hamel, A Michaud, M Thuku, et al. Defining Rapid Reviews: a systematic scoping review and thematic analysis of definitions and defining characteristics of rapid reviews. Submitted to JCE, February 2020.)</td>
</tr>
<tr>
<td>Scoping review</td>
<td>Scoping reviews undertaken with the objective of providing a 'map' of the available evidence can be undertaken as a preliminary exercise prior to the conduct of a systematic review</td>
</tr>
<tr>
<td>Systematic review</td>
<td>A systematic review is a review of a clearly formulated question that uses systematic and reproducible methods to identify, select and critically appraise all relevant research, and to collect and analyse data from the studies that are included in the review. Definition of QES – do we add this? Systematic reviews of diagnostic test accuracy (DTA) summarize the evidence about test accuracy</td>
</tr>
<tr>
<td>Living systematic review</td>
<td>Cochrane has defined living reviews as ‘a systematic review that is continually updated, incorporating relevant new evidence as it becomes available’.</td>
</tr>
</tbody>
</table>
This flow diagram highlights key steps (blue blocks) in the overarching process (in green) with proposed tools to link to in grey.

1. **Determining need for a review**
   - If you identified a good quality, up-to-date review
     - Link to recommending working group resources
   - If you identified an existing review - not up-to-date or of poor quality
     - Resources on updating SR
     - When to consider replicating
   - If you found no existing reviews & decide to conduct a new review
     - Resources on: Clarify question, Registering reviews, Conducting rapid reviews, scoping reviews, SR, living SR. Reporting guidelines

2. **Review update**
   - Conducting a review

3. **What is the issue / decision to be informed?**
   - Link to taxonomy of decisions linked to COVID-19

4. **Identify and appraise existing reviews**
   - Sources of completed living SR, full SR, rapid reviews, evidence profiles
   - Sources of ongoing reviews
   - Tools on how to read SR

5. **Use review to inform decisions**
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.

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.

2.2.1 Access and assess existing evidence synthesis
Identifying the reviews and evidence syntheses that already exist is an essential first step. COVID-END has identified many of the most important searchable databases that already include published systematic reviews.

<table>
<thead>
<tr>
<th>‘Living’ systematic reviews (and derivative products)</th>
</tr>
</thead>
<tbody>
<tr>
<td>o U.S. Veterans’ Affairs (VA) Evidence Synthesis Program - Inventory of living (and regular) systematic reviews (completed and in progress), with a flag for living reviews and for reviews meeting minimum quality standards</td>
</tr>
<tr>
<td>o 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)</td>
</tr>
<tr>
<td>o 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).</td>
</tr>
<tr>
<td>o Campbell Collaboration - Blog profiling Campbell reviews that are relevant to COVID-19</td>
</tr>
<tr>
<td>o COVID-19+ by McMaster PLUS (includes critically appraised systematic reviews and single studies organized by quality level and document type)</td>
</tr>
<tr>
<td>o DistillerSR (includes curated, tagged and downloadable references to single studies)</td>
</tr>
<tr>
<td>o L*VE by Epistemonikos (includes existing systematic reviews of effects and the primary studies, including trials, that were included in the reviews)</td>
</tr>
<tr>
<td>o LitCovid from PubMed (includes systematic reviews and single studies organized by mechanism, transmission, treatment, case report, and epidemic forecasting)</td>
</tr>
<tr>
<td>o Literature Review (includes manually identified systematic reviews and single studies organized by topic and medical specialty)</td>
</tr>
<tr>
<td>o TRIP database (includes systematic reviews and single studies organized by document type)</td>
</tr>
<tr>
<td>o 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</td>
</tr>
<tr>
<td>o McMaster Optimal Aging Portal - Citizen-targeted summaries of systematic reviews that may be relevant to staying active and engaged while practicing physical distancing</td>
</tr>
</tbody>
</table>
There are a number of resources that can be used to evaluate the quality or reliability of published reviews or evidence syntheses.

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

- Article
- Tool
- Guidance

Where high quality 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 be out of date. In such cases an update may represent a more useful and efficient contribution to the research literature than a review that starts from scratch. You may consider approaching the existing authors to determine whether they are intending to update the review before deciding whether to proceed yourself.

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 quality of conduct or reporting. Conscious replication of reviews in such instances is fully justifiable.

### 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
- Cochrane
- **International Platform of Registered Systematic Reviews and Meta-Analysis Protocols** (users can search for free, but registering requires payment) [https://inplasy.com](https://inplasy.com)
- Centre for Evidence Based Medicine (CEBM): Rapid Reviews as part of **Oxford COVID-19 Evidence Service**: Current questions under review

### 3. Conducting new evidence synthesis

If you cannot find a relevant and high quality up to date evidence synthesis, or you have a rationale for replication an existing evidence synthesis, follow this guidance to ensure a robust product.

#### 3.1 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 beneficial. In almost all cases, exploration of this with the appropriate decision makers and any sponsors of the research will improve the quality and utility of the output. There are a number of resources that can help you to make these decisions.
3.1.1 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](https://covidrapidreviews.cochrane.org/search/site)

3.1.2 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?**

3.2 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. Of course, any one individual may bring more than one of these attributes, but conducting high quality systematic reviews require a team approach.

3.3 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.

<table>
<thead>
<tr>
<th>Tool</th>
<th>Link</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Covidence</td>
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<tr>
<td>Distiller SR</td>
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<tr>
<td>Epistemonikos / LOVE tool</td>
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<td>EPPI tool</td>
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<tr>
<td>JBI tool</td>
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<tr>
<td>ReviewManager</td>
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</table>
Automation tools: The following aim to utilize data mining and automated approaches to facilitate the review process.

<table>
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</thead>
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<tr>
<td>Rayyan</td>
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<tr>
<td>RCT Classifier</td>
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<tr>
<td>Robotreviewer</td>
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</table>

Guideline link tools: These tools aim to provide the linkage between systematic reviews and the guidelines process.

<table>
<thead>
<tr>
<th>Tool</th>
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</tr>
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<tbody>
<tr>
<td>Evidence to Decision Framework</td>
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<tr>
<td>GRADEPro</td>
<td></td>
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<tr>
<td>MAGIC</td>
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<tr>
<td>WHO-Integrate Framework</td>
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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.

3.4 Register your title
You may consider submitting your proposed title to 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). In order to assist others, you should register your review protocol in the registries described above. Cochrane reviews are automatically registered on PROSPERO.

3.5 Sources of primary studies
3.5.1 Sources of primary studies on COVID

- **Cochrane COVID-19 Study Register** (includes all study types relevant to Cochrane reviews)
- **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)
3.5.2 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)

3.5.3 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

3.6 Methods for conducting rapid reviews

In some cases, the decision around the type of study is determined by circumstances or the expectations of the sponsor or funder. 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. Both the McMaster Health Forum and the New South Wales Agency for Clinical Innovation have adapted rapid response programs to respond to COVID-19 evidence needs.

‘Rapid reviews’ should be distinguished from conventional reviews conducted rapidly. Over the past decade there has been a rapid increase in activity and interest in the use of digital technologies and crowd based methods to accelerate the review process. The reviews do not seek to ‘streamline or omit’ key methods but aim to conduct these activities more efficiently.

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
3.7 Methods for conducting scoping reviews

JBI - [https://wiki.joannabriggs.org/display/MANUAL/Chapter+11%3A+Scoping+reviews](https://wiki.joannabriggs.org/display/MANUAL/Chapter+11%3A+Scoping+reviews)

3.8 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 Guides and Handbooks:*
- [Cochrane Handbook for Systematic Reviews of Interventions](https://handbook.cochrane.org)
- [Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy](https://handbook.cochrane.org)
- [Methods Expectations for Cochrane Intervention Reviews (MECIR)](https://handbook.cochrane.org)

**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](https://www.campbellcollaboration.org/)

**Agency for Healthcare Research and Quality**
- [Methods Guide for Effectiveness and Comparative Effectiveness Reviews](https://www.ahrq.gov/)

3.9 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](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.

3.10 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 than 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.
3.11 Guidance for reporting of the review

**Equator Network** - Equator aims to improve the quality of reporting of scientific research by the development and communication of reporting standards. Multiple reporting guidelines and their extensions have been produced, including many that apply to evidence syntheses. These include the **PRISMA** guidelines (Preferred Reporting Items for Systematic Reviews and Meta-Analyses), and extensions that 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