Guidance for the production and publication of Cochrane living systematic reviews: Cochrane Reviews in living mode

Version December 2019



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1 Introduction to the guidance

The Cochrane living systematic reviews: Interim guidance for pilots (Version 0.3) was released in April 2017 to guide Cochrane authors and editorial groups involved in the pilot of Cochrane living systematic reviews. The interim guidance was subsequently revised and renamed Guidance for the production and publication of Cochrane living systematic reviews: Cochrane Reviews in living mode (Version 1.0) and released in December 2019.

The core guidance for producing and publishing Cochrane living systematic reviews (LSRs) remains largely unchanged. However, based on our learning from the LSR pilot, this version of the guidance includes updated and/or additional sections on: LSR enablers; managing searches; informing readers about the currency of LSRs; implications for peer review, copy-editing and quality screening; language translation of LSRs; periodic review of an LSR; authorship; transitioning an LSR out of living mode; and resources for Cochrane LSR teams. Appendix 2 includes an updated template for a Cochrane LSR protocol and a new template for a Cochrane LSR.

The purpose of the guidance is to outline the methods, production and publication processes for living systematic reviews of interventions published in the *Cochrane Database of Systematic Reviews (CDSR)*. This document is primarily designed to provide practical guidance for authors, information specialists, Review Groups, and Editorial & Methods Department staff involved in producing and publishing Cochrane LSRs. It is intended to complement the Cochrane Handbook (1) and Methodological Expectations of Cochrane Intervention Reviews (MECIR) (2) both of which continue to apply to Cochrane living systematic reviews. While the guidance has been prepared for the Cochrane context, much of the conceptual information included may be relevant to readers involved in producing and publishing LSRs outside Cochrane. Readers interested in learning more about similarities and differences between LSRs published within and outside Cochrane can follow the findings of a living methodological survey of the conduct and reporting of living systematic reviews (3).

The approach described in this guidance is based on:

- literature relevant to living systematic reviews, including a series of papers published in the Journal of Clinical Epidemiology on behalf of the Living Evidence Network (4-7)
- consultation with Living Evidence Network members, both within and external to Cochrane (see <u>Appendix 1</u> for a list of Living Evidence Network members)
- experiences of teams involved in the pilot of Cochrane LSRs (8-12) and
- the formal evaluation of Cochrane and non-Cochrane pilot LSRs (13).

The new evidence ecosystem is evolving quickly. Approaches to producing and publishing LSRs will continue to develop, and we expect this guidance will continue to evolve. We welcome questions and feedback and invite you to share your experiences of using this guidance. Your feedback can assist in shaping future versions.

Questions and feedback about the living systematic review guidance can be sent to: lsr@cochrane.org

1.1 How to use this guidance

This document is designed for individuals with varying Cochrane roles and therefore some sections will be more relevant than others, depending on the reader's role. Table 1 below highlights the likely relevance of each section by role.

The main body of the guidance introduces the concept of living systematic reviews before describing Cochrane LSR production and publication workflow and methods. This is followed by sections on specific aspects of LSRs including: enablers; managing searches; authorship; and transitioning an LSR out of living mode.

Appendix 2 provides an **LSR protocol template** and an **LSR template** that step authors through LSR-specific considerations for RevMan sections and provide suggested text and examples.

TABLE 1: RELEVANCE OF GUIDANCE SECTIONS BY COCHRANE ROLE

Guida	nce Section	Authors	Information Specialists	Cochrane Review Group	Editorial & Methods Department
Garaar				Editors	Staff
2	Introduction to LSRs	***	***	***	***
3	When to do an LSR	***	***	***	**
4.1	Overview of Cochrane LSRs	***	***	***	**
4.2	Planning and publishing LSR methods	***		***	
4.3	Producing and publishing a living systematic review	***		***	
4.4	Informing readers about the currency of LSRs	***	**	***	***
4.5	Implications of LSRs for peer review, copy-editing and screening	**		***	***
4.6	<u>Language translation of LSRs</u>	***		***	***
4.7	Periodic review of a living systematic review	***	***	***	
5	LSR enablers	***	***	**	**
6	Managing searches for LSRs	***	***	**	
7	Authorship and LSRs	***		**	**
8	Transitioning an LSR out of living mode	***		***	
9	Resources for LSR teams	***	**	**	
12	Appendix 2: Templates for Cochrane LSR protocol and Cochrane LSR	***		***	**

Table legend *** Key sections ** Additional information

2 Introduction to living systematic reviews

2.1 Definition of a living systematic review

An LSR is "a systematic review that is continually updated, incorporating relevant new evidence as it becomes available" (4).

Practically, this means that, while they are in living mode, Cochrane LSRs:

- are underpinned by continual, active monitoring of the evidence (i.e. monthly searches of core databases)
- incorporate in a timely manner any new important evidence (i.e. studies, data or other information), as per pre-specified decisions about when the LSR will be updated
- are supported by up-to-date communication about the status of the review and any new evidence that is in the process of being incorporated or yet to be incorporated into the review (4)

Living systematic reviews are an approach to updating reviews, rather than a review type or method (4, 14). Cochrane Reviews may transition in and out of living mode at various points in their lifecycle.

While core review methods are not fundamentally different to other Cochrane Reviews, LSRs additionally include explicit, transparent and pre-specified decisions on:

- how frequently new evidence is sought and screened; and
- when new evidence is incorporated into the review

Detailed guidance about what to pre-specify in an LSR protocol is provided in Appendix 2.

2.2 How do living systematic reviews differ from other approaches to updating reviews?

Table 2 outlines the key differences between LSRs and other approaches to maintaining review currency.

TABLE 2. COMPARISON OF KEY FEATURES OF LSRS WITH OTHER SYSTEMATIC REVIEW APPROACHES

	Living systematic review	Frequently updated review	Rapid review	Standard systematic review
Explicit, pre-defined methods describing search frequency	✓	×	×	×
Explicit, pre-defined methods describing when new evidence is incorporated into the review	√	×	×	×
Continual evidence surveillance	✓	?	×	×
New evidence is immediately flagged for reader or incorporated into review	✓	?	×	×
Standard SR methods (e.g. screening, data extraction and risk of bias assessment)	✓	✓	?	✓

2.3 Why are living systematic reviews needed?

Systematic reviews are a vital link between the results of health research and evidence-based health decision-making. To be useful, systematic reviews must be valid and reliable. This means that the methods employed must be trustworthy, and reviews must reflect all results of relevant research, including the most recently published data.

The original vision for Cochrane was that it would "include a library of trial overviews, which will be updated when new data become available" (15). Cochrane has led the way in systematic review conduct and been committed to updating reviews as necessary, however, achieving the vision of continually maintaining the currency of Cochrane Reviews has proven impossible in practice. Cochrane Reviews often take more than 12 months to complete and are infrequently updated. Like other systematic reviews, this means that Cochrane Reviews risk not incorporating new evidence that might change the review conclusions (16).

Cochrane authors are now encouraged to make more explicit decisions about when and if to update their reviews. The Updating Classification System provides a decision framework that is informed by the impact of incorporating any known new studies, data, information or methods into the review (17). Reviews on particularly 'hot topics', for which the evidence base is emerging or changing and the question is a high priority for decision-makers, may benefit from a continual, living, updating model.

Living systematic reviews, in alignment with Cochrane's updating guidance, offer a new approach to provide evidence on these 'hot topics' that is both trustworthy and current. While similar to frequently updated 'standard' Cochrane Reviews, LSRs aim to achieve a high degree of currency by continual monitoring of the evidence and require authors to make explicit commitments as to the frequency and methods of updating. By harnessing new review production approaches and technologies, LSRs provide an opportunity to realise the original vision of Cochrane.

2.4 Principles underpinning the Cochrane living systematic review model

The following principles were applied in developing the Cochrane living systematic review model:

- Keep the end-user in mind: maximise the utility of Cochrane Reviews at all stages
- Minimise additional workload (for authors, information specialists, peer reviewers, editors, publishers, language translators and others involved in review production and publication)
- Maximise visibility of the latest findings for the reader
- Maximise efficiencies through technology and involving the crowd
- Streamline workflows and editorial processes
- Build on existing processes and platforms, rather than reinventing the wheel
- Focus on workable, not perfect, solutions
- Remain flexible to incorporate new developments in the broader evidence ecosystem

Box 1: Cochrane's living systematic review activities

During 2017-2018, five pilot Cochrane LSRs were published in the *Cochrane Database of Systematic Reviews (CDSR)* (8-12). Cochrane conducted an evaluation of these pilot LSRs and three non-Cochrane LSRs from the perspective of those involved in the production and publication process (e.g. authors, editors, information specialists, peer reviewers) (13). LSRs were found to be an acceptable and feasible approach to keeping high quality evidence synthesis continually up to date (13).

Cochrane is committed to building on the success of the pilot LSRs and supporting all Cochrane Networks to produce and publish LSRs. Increasingly, Cochrane teams are:

- 1. transitioning existing standard systematic reviews to LSRs (8-12), when appropriate
- 2. publishing protocols for new LSRs (18-20) before producing reviews that commence their lifespan as LSRs

Further information about Cochrane's LSR activities can be found at:

- https://community.cochrane.org/review-production/production-resources/livingsystematic-reviews
- https://community.cochrane.org/review-production/production-resources/livingsystematic-reviews/lsrs-cochrane-library

3 When to do a living systematic review

The decision to undertake an LSR includes considering whether the topic is suited to an LSR (i.e. is it worth it?) and whether the necessary resources are available to maintain an LSR (i.e. is it feasible?). As with other Cochrane Reviews, the decision to initiate a new LSR, or transition an existing review into living mode, rests with the editorial base.

3.1 When is a living systematic review worth doing?

The LSR approach is appropriate for a subset of Cochrane Reviews and possibly only for part of their life cycle. Authors and editorial teams need to make an explicit and careful decision about the appropriateness of commencing a new LSR or transitioning an existing review into living mode. Equally, authors and editorial teams need to make explicit and careful decisions about when to transition a review out of living mode.

Consideration of the conditions under which an LSR is appropriate has been informed by recent guidance on updating systematic reviews (21). As described by Elliott and colleagues (4), an LSR is appropriate when <u>all three</u> of the following criteria are met:

i. The review question is a particular priority for decision-making

With current review production and publication systems, LSRs are only appropriate when the topic is sufficiently important to health decision-making to make the allocation of the necessary resources worthwhile.

In considering the importance of a topic, teams can refer to the Cochrane priority reviews list and the guidance note provided by the Cochrane Knowledge Translation Working Group on Priority Setting (22).

Recent access and usage of an existing review can provide an indication of how important the review question is for decision-making. Therefore, when considering whether to transition an existing Cochrane Review to an LSR, review teams can examine article-level metrics of the existing review (e.g. number of downloads and citations; Altmetric score (23)). Similarly, the rate of publications related to a proposed LSR topic in recent years may indicate its importance for health decision-making.

In addition to Cochrane priority reviews, other suitable topics might include rapidly emerging health issues or technologies. For example, participants in Cochrane's evaluation of pilot LSRs identified questions pertaining to disease outbreaks as appropriate topics for LSRs (13).

Ideally, the importance of the question would lead to the LSR being linked to living recommendations, living guidelines, policy statements or other active approaches to translating the results of the review into practice and/or policy. Given the resources required to maintain an LSR, authors and editorial teams are encouraged to explore opportunities for knowledge translation at the outset, including identifying topics in collaboration with external stakeholders (e.g. guideline developers, professional societies, consumer organisations, funders, health technology assessment agencies). It is also helpful to inform Cochrane's knowledge translation team about new LSRs.

ii. There is an important level of uncertainty in the existing evidence

A living systematic review is only likely to be useful when the current body of evidence is uncertain and the answer to the review question is not settled. Uncertainty in Cochrane Reviews is often indicated by the GRADE assessment of the body of evidence. Review conclusions with a high level of certainty (those with the GRADE certainty rating of 'high') are not likely to change with addition of new evidence.

Uncertainty in the existing evidence may also relate to an absence of good quality systematic reviews on the question of interest; gaps in the primary evidence (e.g. lack of studies in particular populations or settings); or changes in the topic area (e.g. new interventions being tested in primary studies).

iii. There is likely to be emerging evidence that will impact on the conclusions of the LSR

An LSR is appropriate when the research field covered by the review is moving relatively quickly and new evidence is being generated that is likely to impact on review conclusions.

The review team may already have a good understanding that new research is expected because of their familiarity with the research field, as well as through other activities such as checking clinical trial registries, corresponding with researchers working in the field of interest and examining relevant conference proceedings. It can be helpful to involve an information specialist in scoping searches and horizon scanning searches for emerging evidence to determine whether a topic meets the criteria for an LSR.

Not only should there be emerging evidence (e.g. trials underway), the nature of such evidence should have the potential to impact on the LSR conclusions, for example, through reducing the level of uncertainty in the existing evidence.

3.2 When is a living systematic review feasible?

All systematic reviews require substantial time and other resource inputs from authors and editorial teams. In addition to the usual resources required to produce a systematic review, LSRs require a sustained commitment for the period that the review remains living. As such, important considerations regarding the feasibility of maintaining an LSR include whether:

- the author team has the capacity, skill, resources and motivation to sustain an ongoing LSR commitment (acknowledging that the author team may evolve over time)
- the editorial base has the resources to support a Cochrane Review as an LSR

Note: For some topics, an LSR approach to updating a review may be more efficient over the lifespan of a review than the standard approach to updating Cochrane Reviews (i.e. intermittent updates that involve substantial resources for limited periods) (13). However, as no research has yet compared the resources required for these two different approaches, a conservative approach to allocating resources is recommended.

The following questions are designed to assist authors and editorial teams in evaluating whether an LSR is feasible in their current circumstances:

- Does the team have access to someone who will take responsibility for project management;
 e.g. distributing workload, including assigning roles among team members and setting
 expectations about associated responsibilities; and providing continual oversight of the LSR process, including coordinating monthly and less frequent tasks to ensure timelines are met?
- Does the team have access to an experienced information specialist, or other search expert, to manage the monthly search process and regularly assess the search methods over the lifespan of the LSR?
- What is the estimated average monthly workload for the LSR team? This should take into account:
 - o how many citations are expected to be retrieved each month
 - o how many new included studies are expected to be found each month
 - o how often it is anticipated that the LSR will be updated (i.e. a new version published)
- What resources (e.g. funding, staffing) are available to both the author and editorial teams to support the ongoing maintenance of the LSR?
- Are two or more authors available to screen search yields on an ongoing (i.e. monthly) basis, and undertake data extraction and risk of bias assessment as needed?
- Will author contributions be stable over time? Are you able to maintain a consistent direction and approach to the review if the available team composition changes?
- Do all authors agree with the plan to manage authorship implications and expectations? (For guidance about authorship issues, see section '7: Authorship and living systematic reviews').
- Would the authors be prepared to handover leadership of the LSR if the team were no longer able to sustain it, and another author team was able and willing?

Before registering a title for a new living systematic review or transitioning an existing Cochrane Review to living mode, availability of the required resources needs to be considered very carefully. LSRs have workload implications for Cochrane Review Group editorial teams, especially Information Specialists, and for other tasks in the editorial process. Further information about LSR workload implications for Information Specialists can be found in section '6: Managing searches for living systematic reviews'. Section '4.5: Implications of living systematic reviews for peer review, copy-editing and screening' provides an overview of implications for others involved in the LSR process.

4 Production and publication workflow and methods

4.1 Overview of Cochrane living systematic reviews

LSR methods have been developed, piloted and evaluated for intervention reviews

• This guidance has been developed with a standard Cochrane intervention review in mind. The Cochrane LSR pilot only included intervention reviews. While the LSR approach may transfer to other review types (e.g. diagnostic or prognostic test accuracy, qualitative, mixed-methods), the complexity of the methods used for other review types was not examined in the pilot. There may be important differences in how an LSR approach can be applied to different review types (e.g. determining whether there is an important level of uncertainty in the evidence or when new evidence is likely to impact on the conclusions of the LSR).

New reviews and existing reviews can be LSRs

• A new Cochrane Review can be set up as an LSR at the outset, or an existing Cochrane Review can be updated and transitioned into living mode.

LSRs build on a standard Cochrane Review

 Whether an author team is publishing a new review, or transitioning an existing review into living mode, there will need to be an up-to-date 'baseline' review to build upon. That is, authors need to produce a baseline review based on an up-to-date search before commencing the process of screening ongoing monthly searches. This baseline review will be either an entirely new review for a new LSR topic or an updated version of an existing Cochrane Review.

An LSR must involve continual evidence surveillance and continual updates regarding the LSR status, and articulate an explicit approach to updating the LSR itself

• LSRs include active, ongoing evidence surveillance (i.e. monthly searches and monitoring of any identified ongoing studies). Each month, readers are informed of the LSR status (e.g. whether the LSR is up to date or whether new relevant studies have been identified and an update is pending). The LSR itself is updated (i.e. a new version is published) when relevant new information (e.g. studies, data) that is likely to impact the conclusions of the LSR is identified *or* on a pre-specified fixed schedule (e.g. every 4 months). Criteria for ceasing continual updates of the LSR (i.e. transitioning an LSR out of living mode) should also be articulated in the protocol.

Core review methods are largely unchanged

• Cochrane LSRs follow the same core methods and review steps as standard Cochrane Reviews. What differs is that additional a priori decisions are made about how the review will be maintained as an LSR, and these are documented in the protocol.

Additional decisions specific to LSRs must be considered

- An LSR requires explicit, transparent and predefined decisions about:
 - o how frequently new evidence is sought and screened
 - Bibliographic databases and clinical trial registries specified in the search strategy should be searched monthly. Other sources (e.g. grey literature, conference proceedings) may be searched less frequently, as specified in the protocol.
 - o when new evidence is incorporated into the review
 - Although searches are conducted monthly, it is currently unfeasible to publish an update to a Cochrane LSR on a monthly basis. Depending on the rate at which new relevant evidence is expected to be found, there are two options for the frequency of updating an LSR
 - 1. Update the LSR when new evidence identified is likely to impact the review conclusions, as shown in Figure 1; or
 - 2. Update the LSR on a fixed-interval schedule when a high volume of new evidence is anticipated. As an example, the Cochrane pilot LSR with the highest rate of new evidence was updated every 4 months during the pilot period (8).
 - o when methods (e.g. search strategy) will be reviewed.
 - o when an LSR will be transitioned out of living mode (*see section '8: Transitioning a living systematic review out of living mode'*).

LSR-specific decisions must be documented a priori

LSR-specific decisions are planned and reported in the relevant sections of the protocol.
 Where an existing standard Cochrane Review is being transitioned into living mode, the LSR-specific aspects must be documented in the relevant sections of the main text and in an appendix to the review that describes the LSR-specific methods.

LSRs use existing publication processes

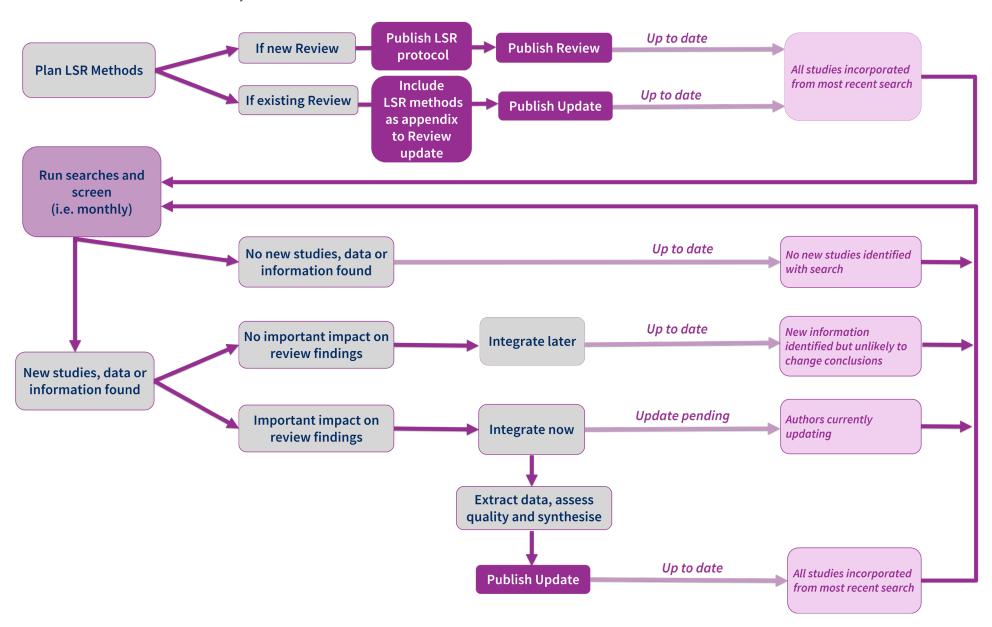
• The Cochrane LSR model makes use of the What's New table as a way to provide LSR status updates to readers, without having to re-publish the Cochrane Review after each monthly search. Guidance on how to use the What's New table is provided in section '4.4: Informing readers about the currency of living systematic reviews'.

The What's New table is currently the preferred mechanism for providing readers with updates regarding the status of an LSR.

• If new evidence is incorporated into the review, the standard updating processes apply and all sections of the review must be updated and republished.

The Cochrane living systematic review model is presented diagrammatically in Figure 1.

FIGURE 1. COCHRANE LSR WORKFLOW, WITH PUBLICATION OUTPUTS



Notes for Figure 1:

- 1. The framework for the workflow is based on the paper by Garner et al published in the BMJ in 2016 (21).
- 2. When a high volume of new evidence is anticipated, a fixed-interval schedule may be more feasible for the authors and editorial team than updating the review each time new evidence that is likely to impact the conclusions is found.
- 3. Until the functionality to publish a new (updated) protocol for an existing review that is being transitioned to an LSR becomes available, the published LSR can describe the LSR-specific methods in the main text, as well as an Appendix entitled "Living systematic review protocol". (See <u>Appendix 2</u> for detailed guidance).

4.2 Planning and publishing living systematic review methods

4.2.1 Registering a title for a new living systematic review

Standard Cochrane processes apply when proposing and registering a new Cochrane Review that will be in living mode; see

https://documentation.cochrane.org/display/EPPR/Cochrane+Review+proposals. The title for a new LSR does not indicate that the review is an LSR. Given that an LSR may transition out of living mode (see section '8: Transitioning a living systematic review out of living mode' for further details), the review title must be appropriate for a standard Cochrane Review. Before registering a title for a new LSR or transitioning an existing Cochrane Review to living mode, availability of the required resources needs to be considered very carefully.

The Managing Editor needs to notify the <u>LSR support team</u> whenever a new LSR title is registered or whenever the CRG has approved the transition of an existing Cochrane Review to living mode. This will allow the LSR support team (and the EMD) to monitor the progress of all Cochrane LSRs.

4.2.2 Planning LSR methods

A protocol for a Cochrane LSR will include all the usual information that is reported in a standard Cochrane protocol. Living systematic reviews also require that additional specific methodological decisions are made and described in the protocol. All LSR-specific methods can be incorporated into the standard headings of a Cochrane protocol and Cochrane Review.

LSR protocols require additional information relating to:

- search methods and frequency (see section '6: Managing searches for living systematic reviews')
- deciding when to integrate new information (e.g. new studies, development of new interventions, additional data for included studies, retraction of an included study); see Box 2 below for guidance around making this decision
- deciding whether and how to retain existing 'legacy' information (e.g. an intervention may no longer be licensed for use)
- deciding when an LSR should be transitioned out of living mode (see section '8:
 Transitioning a living systematic review out of living mode')

Box 2: When to integrate new evidence into a living systematic review

For LSRs where a high volume of new evidence is anticipated, it may be deemed most feasible to specify in the protocol that the LSR results will be updated on a fixed-interval schedule approved by the editorial team (e.g. every four months).

Ideally, however, updates will occur whenever new evidence likely to impact the review conclusions is identified, as shown in Figure 1.

It is important that author teams consult with the editorial team regarding which of the above two options to use.

There are two key methodological issues associated with determining whether new evidence will impact on the conclusions of the LSR. The first relates to whether authors choose to:

apply methods to predict if new evidence is likely to impact the LSR conclusions; or

• incorporate the new data and re-run the data analysis to directly determine whether the LSR conclusions have changed.

The second issue pertains to specifying what type/degree of changes in LSR conclusions are sufficiently important to warrant publication of an updated version of the LSR. Numerical thresholds for changes in findings that might warrant an LSR update (e.g. magnitude of change in effect size or precision of effect size estimates for primary or secondary outcomes) have not been established. Other considerations include whether the new evidence leads to a change in the GRADE certainty rating or the direction of effect, or introduces previously unreported interventions, populations, serious adverse events or other clinically meaningful findings.

Further guidance regarding methods for determining whether new evidence may impact the conclusions of an existing systematic review can be found in an article by Garner and colleagues (24) and Cochrane Handbook Chapters IV (25) and 22 (26). For example, Chapter 22 provides an overview of the Framework for Adaptive Meta-analysis (FAME) (27, 28). FAME takes into account all relevant trials, including those for which results are not yet available, and uses trial information to predict when a reliable aggregate data meta-analysis will be possible.

4.2.3 Publishing LSR methods

The approach to publishing the planned LSR methods for a Cochrane Review varies depending on whether the LSR is a new review, or an existing Cochrane Review is being transitioned into living mode.

For new reviews:

- Authors incorporate the planned LSR methods into the protocol for the review.
- The protocol is published according to standard Cochrane processes, including peer review. The <u>LSR support team</u> can provide peer review of the LSR methods (29).

For existing Cochrane Reviews:

- Authors can send the planned LSR methods to the <u>LSR support team</u> to check prior to updating the review.
- The LSR-specific methods are integrated in the main text, as well as being included as an appendix to the review (see <u>Appendix 2</u> for an example of a 'Living Systematic Review Protocol' appendix).
 - Note: This approach may change when the functionality to publish a new protocol for existing reviews becomes available in the CDSR. In the interim, the LSR-specific methods appendix serves as a substitute for publishing a new protocol.
- If approved for publication, then the Managing Editor will publish the updated review in the CDSR.

Considerations for editorial teams:

 At the protocol planning stage, it is useful for Managing Editors to identify a pool of peer reviewers who agree to review the protocol, baseline review and subsequent updates for a specified duration (perhaps 12 months). In addition, having an information specialist peer review the primary database strategy via a validated assessment instrument (e.g. PRESS guidelines (30)) should also be considered at the protocol stage. Further information about LSR peer review can be found in section '4.5: Implications of living systematic reviews for peer review, copy-editing and screening'.

 Following peer review of an LSR protocol, it is useful for the protocol to be screened by the relevant Network and Associate Editors, given that LSRs are likely to be highly visible reviews (31).

4.3 Producing and publishing a living systematic review

4.3.1 Producing a baseline review

Irrespective of whether the LSR is commenced as a new review or an update to an existing review, there needs to be an up-to-date Cochrane Review published in the *CDSR*. This is referred to as a 'baseline' review. Only after this point will the 'living' part of the LSR commence for the reader.

The baseline review should be conducted in accordance with Cochrane's Methodological Expectations of Cochrane Interventions Reviews (MECIR) guidelines (2), and be published following standard Cochrane processes. All eligible studies should be fully integrated in the review, and the LSR methods should be outlined in the Methods section. Where an existing Cochrane Review is being transitioned into living mode, the baseline review should also include an appendix describing the LSR-specific methods. (See <u>Appendix 2</u> for detailed guidance on reporting the baseline review.)

4.3.2 Publishing the baseline review

After peer review, Managing Editors can send the baseline review to the Network Associate Editor for quality screening. In addition, LSRs that are not copy-edited by the Cochrane Review Group should be sent to Copy Edit Support. Given the necessity for rapid processing times for LSRs, it is important that discussions are held well in advance, to agree the turnaround time for LSRs. Further considerations regarding LSR publishing workflows are outlined in section '4.5: Implications of living systematic reviews for peer review, copy-editing and screening'.

The Managing Editor applies the What's New events applicable to the baseline review at the time of publication. The review may not be up to date if searches conducted since the baseline review search have identified new evidence that will be incorporated in the next version of the LSR. For further details on applying What's New events to the baseline review, see section '4.4: Informing readers about the currency of living systematic reviews'.

4.3.3 Preparing for the transition to living mode

Once the 'baseline' review is published, the review immediately becomes a living systematic review in the *CDSR*.

The Managing Editor can return the review to authoring mode in RevMan. This will allow the authors to make any updates to the material over time (e.g. PRISMA, characteristics of excluded studies), so that when the time comes to re-publish the review, most of the new evidence will already have been incorporated.

Maintaining an LSR will require the coordination of multiple recurring tasks associated with various versions of the LSR. Before transitioning to living mode, author teams need to consider which processes they will put in place to manage concurrent tasks associated with different versions of the LSR. For example, teams may be addressing peer review comments for the next version to be published, while also working on the data synthesis section for a subsequent version at the same time as conducting ongoing screening of titles/abstracts. Accordingly, effective version control of data, documents and other files is crucial.

4.3.4 Once the review is in living mode

The ongoing searches are run and screened at their pre-specified frequency (i.e. monthly for bibliographic databases and clinical trial registries, and typically less frequently for other sources). The team may have commenced the monthly searches some months earlier (e.g. setting up bibliographic database auto-alerts immediately following execution of the search for the baseline review), in anticipation of the review becoming living. For further details about setting up ongoing searches, see section '6: Managing searches for living systematic reviews'.

Each month, the authors advise the Managing Editor within the month (i.e. before they receive the search yield for the next month) of the outcome of screening the monthly search yield, as per the three scenarios described below. In turn, the Managing Editor updates the What's New table to communicate to the reader the current status of the LSR. (For details on using the What's New table, see section '4.4: Informing readers about the currency of living systematic reviews').

The LSR is updated according to the decisions specified in the protocol. Ideally, updates will occur whenever new evidence likely to impact the review conclusions is identified, as shown in Figure 1. For LSRs where a high volume of new evidence is anticipated, however, it may have been deemed more feasible to specify in the protocol that the LSR results will be updated on a fixed-interval schedule approved by the editorial team (e.g. every four months). The procedures for each of these two options are described below. (For guidance on deciding when to update an LSR, see 'Box 2: When to integrate new evidence into a living systematic review').

4.3.4.1 Updating LSRs whenever new evidence is likely to impact review conclusions In the case of an LSR for which the timing of updates is determined by the impact of evidence on the review conclusions, there are three possible scenarios arising from screening the ongoing search yields, as shown in Figure 1. Each scenario has different implications for the authors and Managing Editor, the way in which RevMan is used, the need for peer and editorial review, and information recorded in the What's New table. The detail below supplements the information provided in Table 3. (For the current information about using What's New/publishing events, please see the Cochrane Editorial and Publishing Policy Resource section: https://documentation.cochrane.org/pages/viewpage.action?pageId=117380266.)

Scenario 1: No new evidence (studies, data, information) is identified

 The review conclusions remain up to date and the Managing Editor adds a What's New "Amended" event with the description field indicating the most recent search date.

Scenario 2: New evidence is identified but is unlikely to have an important impact on review findings and will be integrated later.

The review conclusions can be considered up to date.

- This option should have been pre-specified in the Methods section of the protocol, with specific decision rules pre-specified. The authors' decision not to integrate new evidence should be justified and requires editorial review and approval. Cochrane Review Group Editors review the authors' decision not to integrate the new evidence and may seek the opinion of a peer reviewer.
- Once confirmed, the Managing Editor adds an "Amended" event using the What's New table, with the description field indicating the most recent search date and stating how many studies are pending inclusion in the LSR.

Scenario 3: New evidence is identified that is likely to have an important impact on review findings.

- A full update of the review is undertaken in line with MECIR standards (2).
- This scenario can be regarded as comprising two stages. As shown in Table 3, integrating the new evidence (Stage 1) and then publishing an update (Stage 2) have different implications for author and editorial activities, RevMan, the What's New table and the CDSR.
- **During Stage 1** (i.e. before the update is published), the What's New table is used to flag to readers that the authors are integrating new evidence and an update is pending. The Managing Editor adds a What's New "Amended" event to indicate that the authors are currently updating the review. The What's New Description field can be used to specify the most recent search date; provide information about the new evidence (e.g. number of new studies found; DOIs of new studies); and the month-year when the update is expected to be published.
- **Note:** Unlike an update for a standard Cochrane Review, the monthly searches continue to be run and screened while the new evidence is being integrated and the update published. Accordingly, after each monthly search, a What's New "Amended" event needs to be added with the description field stating that an update is being prepared with XX studies found up to the last search date applicable to the update in progress AND the outcome of subsequent monthly searches. That is, the status of ongoing search results must continue to be updated each month.
- **During Stage 2** (i.e. publishing the update) Managing Editors may wish to consider using the same group of peer reviewers for all versions of the LSR or a designated period of time (e.g. 12 months). As with the baseline review, it is important that Managing Editors give the Network Associate Editor advance notice of the LSR's arrival. In addition, LSRs that are not copy-edited by the Cochrane Review Group should be forwarded to Copy Edit Support with advance notice. Providing those checking the LSR with a 'compare' version will allow them to see what has changed since the last update (32). On publishing the update, the What's New table must be updated to reflect the current status of the LSR (See Table 3: Note 4).

For each of the scenarios described above, Table 3 outlines the activities of authors and Managing Editors, the way in which RevMan is used, the need for peer and editorial review, and the publication and What's New table implications.

TABLE 3. AUTHOR AND EDITORIAL ACTIVITIES FOR THE LSR SCENARIOS ARISING FROM SCREENING ONGOING SEARCHES¹

		Once the review become	omes living		
		Scenario 1: No new evidence identified	Scenario 2: New evidence, No important impact, integrate later	Scenario 3: Stage 1 New evidence, important impact, integration in process	Scenario 3: Stage 2 New evidence, important impact, publish the update
	Alert Managing Editor	✓	✓	✓	✓
or ities	Edit RevMan file	✓	✓	✓	✓
Author Activities	Submit RevMan file	*	×	×	✓
RevMan	RevMan file (mode)	Authoring	Authoring	Authoring	Authoring to Editorial, then Publish; return to Authoring ²
	ME adds What's New event and description to indicate LSR status ³	Amended event; No new studies identified with search	Amended event; New information identified but unlikely to change conclusions	Amended event; Authors currently updating	All studies incorporated from most recent search Or New information identified but unlikely to change conclusions or Authors currently updating ⁴
Se	Editorial review?	×	CRG editors review authors' decision	×	✓
Editorial activities	Peer review?	×	? (if req'd for second opinion)	*	✓ (in line with peer review policy)
Editorial	Cochrane Review publication	Unchanged	Unchanged	Unchanged	Update

Abbreviations: LSR = Living Systematic Review, RevMan = Review Manager, ME = Managing Editor

Notes:

- 1. Table 3 describes potential scenarios that may arise when screening the ongoing search yields for LSRs that are updated whenever new evidence is likely to impact review conclusions
- 2. After an update to the LSR is published, the Managing Editor can return it to Authoring mode in RevMan so that the authors can continue working on the LSR (e.g. adding new data into the tables for included studies and excluded studies; updating PRISMA) in preparation for the next update
- 3. For detailed guidance on using the What's New table for LSR status updates, see section '<u>4.4: Informing readers about the currency of living systematic reviews'</u>. Also see the Cochrane Editorial and Publishing Policy Resource for the current guidance on applying What's New/publishing events for Cochrane Reviews: https://documentation.cochrane.org/pages/viewpage.action?pageId=117380266.
- 4. An updated version of the LSR may not be up to date when published, if subsequent monthly searches have yielded additional eligible studies that are currently being integrated for publication in a future update

4.3.4.2 Updating LSRs on a fixed-interval schedule

In the case of an LSR that is updated on a fixed-interval schedule, scenarios arising from screening the ongoing search yields will often be like those described above for LSRs that are updated whenever identified evidence is likely to change review conclusions.

However, LSR teams will also need to decide whether they would proceed with an update in the following two scenarios and pre-specify these decisions in the protocol:

- A scheduled update is due to be undertaken, but the ongoing searches have identified no new evidence.
- 2. A scheduled update is due to be undertaken, but the ongoing searches have only identified new evidence that is unlikely to change the review conclusions.

4.4 Informing readers about the currency of living systematic reviews

A key finding of the evaluation of Cochrane pilot LSRs was the need to provide CDSR users with helpful information about the status of an LSR. The What's New Description field can be used to convey information about new evidence yet to be incorporated into an LSR; e.g. the most recent search date; the number of new studies identified; and DOIs of these studies.

4.4.1 What's New Table

The What's New table comprises three fields: date, event type, and description. (See details in the Cochrane Editorial and Publishing Policy Resource:

https://documentation.cochrane.org/pages/viewpage.action?pageId=117380266)

Notes:

- To maintain transparency regarding the outcomes of continual monthly searches for an LSR, all What's New events must be moved to the History section, rather than being overwritten.
- The use of the What's New table to provide LSR status updates, as described below, is an exception to Cochrane policy on the use of the What's New table that is specific to LSRs.

4.4.1.1 What's New table for the LSR baseline review

The What's New events and description will vary according to whether:

- 1. the LSR is an entirely new Cochrane Review or an existing Cochrane Review that has been updated in preparation for transitioning into living mode. Standard Cochrane policy can be followed to add a What's New table entry describing changes between the previous version of an existing Cochrane Review and the LSR baseline review.
- 2. the baseline review is up to date at the time of publication. A What's New table entry can be added to indicate the outcome of any searches that have occurred since the date of the search used to prepare the baseline LSR.

Example 1: Baseline review is up to date at the time of publication

What's New event	Amended
What's New	This is a Living Systematic Review. Searches are run and screened
description	monthly. Last search date 30 November 2019. Results of all new
	studies identified have been incorporated. The conclusions of this
	Cochrane Review are therefore considered up to date.

Example 2: Baseline review is not up to date at the time of publication, as ongoing monthly searches have identified new evidence that is likely to change the review conclusions

What's New event	Amended
Explanation	This is a Living Systematic Review. Searches are run and screened monthly. The next update, with search results to 27 April 2019 (2 new studies, 3 new ongoing studies), is due in July 2019. As of the last search (27 June 2019) there are also 2 additional new studies to be included after the July 2019 update and 4 new ongoing studies.

4.4.1.2 What's New table for LSRs that are updated whenever new evidence is likely to impact review conclusions

Below are examples of What's New events and descriptions that could be entered for each of the scenarios listed in Table 3.

Scenario 1: No new evidence identified in monthly search yield

What's New event	Amended
What's New	This is a Living Systematic Review. Searches are run and screened
description	monthly. Last search date 15 June 2019. Results of all included
	studies identified have been incorporated. The conclusions of this
	Cochrane Review are therefore considered up to date.

Scenario 2: New evidence identified in monthly search yield but has no important impact on review findings; integrate later

What's New event	Amended
What's New	This is a Living Systematic Review. Searches are run and
description	screened monthly. One study has been found in searches up to 15 June 2019 (hyperlink to DOI XXX) but is unlikely to change review conclusions (as assessed by the authors and editorial team). The conclusions of this review are therefore considered up to date.

Scenario 3-Stage 1: New evidence identified in monthly search yield which has an important impact on review findings; integration in progress

<u>Example 1</u>: No new evidence is found by ongoing monthly searches while the authors are preparing an update to the review

What's New event	Amended
What's New description	This is a Living Systematic Review. Searches are run and screened monthly. The next update, with results to 27 April 2019 search (1 study, hyperlink to DOI XXX), is due in July 2019. Screening of monthly searches continues (last search date 27 May 2019) and has found no additional new evidence.

<u>Example 2</u>: New evidence is found by ongoing monthly searches while the authors are preparing an update to the review

What's New event	Amended
What's New description	This is a Living Systematic Review. Searches are run and screened monthly. The next update, with results up to 27 April 2019 search (3 new studies, 2 new ongoing studies), is due in July 2019. Screening of monthly searches continues (last search date 27 June 2019) and has found 2 additional new studies to be included after the July 2019 update and 4 new ongoing studies.

Scenario 3-Stage 2: New studies identified, likely to change conclusions, publish the update

The fact that a new version of the review has been published will be captured in the What's New table, as per standard process for an updated review.

Another What's New event can be added to indicate that outcome of ongoing searches that have occurred while the update was being produced and published, as per below.

<u>Example 1:</u> No new evidence was found by ongoing monthly searches while the current update was being produced and published

What's New event	Amended
What's New	This is a Living Systematic Review. Searches are run and
description	screened monthly. Last search date 27 June 2019. Results of all
	new studies identified have been incorporated. The
	conclusions of this review are therefore considered up to date.

<u>Example 2:</u> New evidence has been found by ongoing monthly searches while the current update was being produced and published, such that the current update is not "up to date" at the time of publication

What's New event	Amended
What's New	This is a Living Systematic Review. Searches are run and
description	screened monthly. The next update, with results up to 27 May
	2019 search (2 new studies [hyperlink to DOI XXX; DOI YYY], 3
	new ongoing studies), is due in July 2019. Screening of monthly
	searches continues (last search date 27 June 2019) and has
	found no additional new evidence.

4.4.1.3 What's New table for LSRs that are updated on a fixed-interval schedule
In the case of an LSR that is updated on a fixed-interval schedule, the scenarios arising from
screening the ongoing searches will be similar to those for LSRs that are updated whenever new
evidence is identified, as described above. As such, the examples above can be used to guide use
of the What's New table for LSRs updated on a fixed-interval schedule.

In addition, the following scenarios may arise for such LSRs:

- 1. A scheduled update is due to be undertaken, but the ongoing searches have identified no new evidence.
 - a. Teams may have decided to skip the scheduled update in such a scenario, rather than publishing a new LSR version which would, in turn, generate a new citation version.
 - b. If the decision was made to skip an update when no new evidence has been found, a What's New "amended" event would be added, and the description field would be used to inform the reader of the date of the last search and that no new evidence has been found.

- 2. A scheduled update is due to be undertaken, but the ongoing searches have only identified new evidence that is unlikely to change the review conclusions.
 - o If the decision was made to skip an update in such a scenario, a What's New "amended" event would be entered and the description field used to inform the reader about the number and DOIs of newly identified studies, the date of the last search, and that the new evidence is unlikely to change the review conclusions.

4.5 Implications of living systematic reviews for peer review, copy-editing and screening

4.5.1 Peer review of living systematic reviews

Peer review of LSRs must comply with the Cochrane peer review policy (33). At the protocol stage, it can be beneficial for Managing Editors to identify a pool of peer reviewers who agree to review the protocol, baseline review and subsequent updates. Given the potentially long period for which an LSR might remain in living mode, it can be helpful to ascertain the duration for which peer reviewers anticipate they can be available. If it is not possible to retain the same set of peer reviewers over the lifespan of the LSR, sending new peer reviewers key points from prior peer review reports can help maintain consistency of feedback to authors across different peer reviewers (33).

The evaluation of the pilot Cochrane LSRs found that peer reviewers wanted guidance on how to approach an LSR peer review (13). It can be helpful for Managing Editors to provide potential peer reviewers with some information about LSRs (e.g. LSR definition, LSR protocol template and LSR template included in this guidance). It is also important to discuss the anticipated workload of peer reviewers (e.g. how often new updates will be produced and whether these would require full/specialised/no peer review), and agree on turn-around times for LSR peer review.

Selective peer review of only those parts of the LSR that have changed from the previous version can ease the burden on peer reviewers and support the timely completion of peer reviews required for the LSR model. Providing peer reviewers with a 'compare' version will allow them to see what has changed since the last LSR update (32).

The need for full versus selective peer review should be made in accordance with the Cochrane peer review policy (33). Consistent with this policy, Managing Editors can invite peer reviewers to focus on particular components of the LSR relevant to their expertise.

The <u>LSR support team</u> is available to peer review LSR-specific methods of protocols and reviews. Information specialists with experience in living evidence surveillance methods could be invited to peer review LSR search methods. Statisticians with expertise in repeated multiple intervention comparisons can peer review LSRs that involve living network meta-analysis. Editors can contact the <u>LSR support team</u> for assistance with identifying peer reviewers for LSR-related aspects of protocols and reviews.

4.5.2 Copy-editing living systematic reviews

Cochrane's policy is that all new and updated Cochrane Reviews must be copy-edited before publication. Given the tight time frames underpinning the LSR model, Managing Editors must provide Cochrane Copy Edit Support or their Group's accredited copy-editor with advanced notice of the pending arrival of an LSR. The evaluation of Cochrane pilot LSRs found that the time required for copy-editing decreased across subsequent versions of an LSR. Copy-editors will usually focus chiefly on content that has changed in the new version of the LSR, but will also consider the update as a whole (32), and additional full copy-edits of LSRs will be completed as required, potentially annually.

4.5.3 Screening living systematic reviews

In this context, "screening" refers to Cochrane's pre-publication quality assurance programme which involves checking the quality of protocols and systematic reviews against key criteria prior to publication. Given the LSR approach will be applied to topics of high priority to decision-makers and therefore potentially highly visible, it can be beneficial if the Network Associate Editor screens LSR protocols and LSRs, particularly when there have been substantive changes from previous versions. It is also important to follow screening requirements for the applicable Cochrane Network and inform Senior Network Editors about new LSRs (31).

The evaluation of Cochrane pilot LSRs found that LSR screening time was comparable to standard Cochrane Reviews. Identified opportunities for reducing screening time included using the triage tool to facilitate the same person undertaking the screening across different versions of a given LSR, thereby increasing familiarity with the content (13). Similar to the peer review and copy-editing processes, a 'compare version' can assist in identifying changes for a new version, as well as text that authors may have omitted to change. It is also helpful if Managing Editors provide advance notice of the arrival of an LSR update to the Network Associate Editor, and forewarning of whether a more intensive screening process may be required because the evidence base has changed considerably since the last update.

4.6 Language translation of living systematic reviews

Cochrane Reviews are currently being translated into up to 15 languages (34). Translation of Reviews currently involves translation of the Abstract and/or Plain Language Summary, at a minimum. Translations into Spanish often also include main text sections. Note that the What's New event descriptions are not currently translated.

To facilitate translation of LSRs, it is useful if authors and Managing Editors

- use standard text, as appropriate, across LSR versions (e.g. using the suggested text for the Editorial note included in the Abstract and Plain Language Summary [see the LSR template in Appendix 2]; and What's New Description field;
- use simple and plain language avoiding complex sentence structures, grammar and ambiguities, where possible and appropriate; and
- edit the text of Abstract, Plain Language Summary and main text when required only;
 non-essential copy-edits should be delayed to the next update of the LSR.

The use of standard text and plain language reduces the resources required for human translators, and facilitates the application of artificial intelligence tools including translation memory and machine translation. In translation editor software, typically, similar or identical

sentences that have been translated previously, will be suggested automatically to translators (via the so called "translation memory"). Likewise, suggestions from machine translation engines are usually shown directly in the translation editor, and those perform much better, if text follows basic simple and plain language recommendations, as much as possible (short sentences, one statement per sentence, active instead of passive voice, remove filler words, avoid metaphors and figural speech, avoid complicated syntax, avoid slang and jargon, etc.)

4.7 Periodic review of a living systematic review

After an LSR has been in living mode for 12 months, a review of the following aspects of the review is recommended:

- 1. Appropriateness of continuing to maintain the review in living mode.
 - See section '8: Transitioning a living systematic review out of living mode' for guidance regarding factors to consider in determining whether a living approach to the review is still appropriate.

2. Methods

- Search strategy (see section '6: Managing searches for living systematic reviews').
- Have any new relevant methods emerged that would be appropriate to integrate into the methods? Examples include risk of bias tools, statistical techniques and technological enablers.

3. Author team

• It is important to consider which authors will work on the LSR over the next 12 months and set expectations about the criteria for authorship. See section '7: Authorship and living systematic reviews'.

4. Peer reviewers

• If a consistent team of peer reviewers has been involved in the LSR over the past 12 months, it can be helpful for the Managing Editor to inquire whether they will be available for the next 12 months.

5 Living systematic review enablers

While Cochrane has always aspired to produce "a library of trial overviews, which will be updated when new data become available" (15), the extensive time, effort and skill required have been persistent barriers to achieving this vision. However, recent innovations can substantially reduce and potentially overcome these barriers. Table 4 lists some innovative enablers that may improve the efficiency of producing an LSR baseline review and continual LSR maintenance. This list is not exhaustive and LSR teams can find a wider range of enablers through sources such as the Systematic Review Toolbox (35).

Enablers offer potential efficiency gains for many stages of LSR production (7). For example, the work involved in conducting ongoing searches can be reduced by setting up automated searches in bibliographic databases. Text mining, machine learning and other forms of automation, along with citizen science platforms, can substantially reduce the burden of screening search results. Author support tools including online task sharing tools provide opportunities to support and manage diverse contributor teams. New approaches to quality assurance and publication enable rapid publication of high-quality reviews. Each of these innovations presents an opportunity to produce better reviews quicker.

Cochrane has developed key enablers of LSRs such as text mining and machine learning tools (e.g. RCT classifier), citizen science platforms (e.g. Cochrane Crowd (36)), systems that seamlessly integrate multiple enablers (e.g. Screen4Me), and Cochrane's Author Support Tools (e.g. Covidence (37), TaskExchange (38)). These and other enablers make it possible to continually assess and curate the evidence base for Cochrane LSRs in a systematic, efficient and collaborative way.

At the protocol planning stage, authors and information specialists can identify enablers that will be used to produce the baseline review and/or support the ongoing maintenance of the LSR. Any use of enablers must be compliant with MECIR standards (2). Tools listed in Table 4 that do not require Cochrane Scientific Committee approval include Cochrane Crowd; TaskExchange; Covidence; EPPI-Reviewer; Rayyan; RCT classifier; Screen4Me; Project Transform Evidence Pipeline; CrossRef; SRA-Helper; RevManHAL; and RevMan Replicant. Authors wishing to use other tools can <u>submit a request to Cochrane's Scientific Committee</u> so that the tools can be considered for use in Cochrane Reviews.

The LSR protocol should describe which tools will be used, for what tasks and how they will be implemented. Similarly, the LSR itself should report how tools were used.

TABLE 4. LSR ENABLERS [ADAPTED FROM THOMAS ET AL (7) AND ELLIOTT ET AL (39)]

Review Task Category	Method/Task	Enablers
Establishing the team and processes for collaboration	Forming a large and diverse group of contributors	Crowd participation, citizen science and task- sharing platforms (e.g. Cochrane Crowd; TaskExchange) enable distribution of tasks among a large team.
	Establishing mechanisms for collaboration among team members	Workflow management and collaboration tools include Covidence, EPPI-Reviewer (40) and Rayyan (41).
Production	Searching	Many bibliographic databases support automated email alerts (auto-alerts) of new results for saved searches.
	Assessing studies for eligibility	During abstract/title screening RCTs can be identified using machine learning algorithms (e.g. RCT classifier), crowd-sourcing (e.g. Cochrane Crowd) and integrated systems (e.g. Screen4Me; Project Transform Evidence Pipeline (42)). Retrieval of full-text reports can be automated or accelerated (e.g. CrossRef; SRA-Helper (43, 44)).
	Extracting data	Machine-learning and automated structured data extraction tools collect information about PICO components and/or risk of bias (e.g. RobotReviewer; ContentMine; Graph2Data)
	Data synthesis and writing up	Enablers for data synthesis are in the early stages of development. Automatic text generation tools include RevManHAL (45) and RevMan Replicant (46).
Publication	Peer and editorial review	Cochrane peer review policy permits peer reviewers to focus on reviewing changed sections of an LSR, rather than the entire manuscript (33). Archie compare function enables reviewers and editors to identify changes between LSR versions (32).
	Dissemination and communicating to users	Authors can inform users about the status of LSR currency from month to month (including the most recent search date and links to new studies which have been identified but not yet incorporated) using the What's New table.

It can be helpful to estimate the average number of records expected in monthly searches when deciding whether to use enablers in managing the workload of maintaining the LSR from month to month. In determining which enablers to use, LSR teams are encouraged to consider any limitations on the use of various tools. For example, at the time of finalising this guidance document, some Cochrane enablers (e.g. RCT classifier) were available to Cochrane information specialists only.

Some technological enablers are further developed and validated than others. Therefore, it is helpful to consult the evaluation literature to understand the strengths and limitations of available tools. For example, it is important to consider any limitations on the accuracy of screening or data extraction tools in the context of risk tolerance for errors. The Cochrane <u>LSR support team maintains an LSR Mendeley library</u> to which we regularly add new literature on various aspects of living evidence, including evaluations of technological enablers.

The development of systematic review enablers is progressing steadily within Cochrane and other organisations. Accordingly, review teams may benefit from keeping up to date with websites and scholarly literature on emerging enablers that could be incorporated into a revision of LSR methods (e.g. 35, 47, 48). For instance, work is underway within Cochrane to develop machine learning algorithms to classify studies according to PICO components. In addition, functionality for a living PRISMA flow diagram will soon be available to Covidence users. As another example, the Cochrane Linked Data Project offers a repository of structured systematic review data that could be harnessed to increase the efficiency of LSR maintenance, particularly for assessing study eligibility.

6 Managing searches for living systematic reviews

Regular searches and timely screening of search results are key characteristics of living systematic reviews. It is highly recommended that LSR teams include an information specialist to establish and manage evidence surveillance to ensure the efficiency and validity of the search.

In the evaluation of pilot LSRs the time spent by information specialists processing monthly search updates ranged from 30 minutes to 6 hours. It is important information specialists are aware of the increased workload, and account for it. Depending on the scope of the review and the number of records retrieved each month, technological enablers may improve efficiency compared to traditional approaches to managing search results. Access to many of these enablers (e.g. Screen4Me, RCT classifier, Cochrane Crowd) will require the involvement of a Cochrane information specialist.

Box 3: Why information specialists are needed

These are some of the key roles of information specialists at different stages of an LSR:

- Protocol: estimate the likely size of monthly search results and advise on the suitability of technological enablers (e.g. RCT classifier, Cochrane Crowd, Screen4Me) to increase the efficiency of the search.
- Transition baseline review to living mode: set up monthly searches (e.g. using database auto-alerts), establish comprehensive workflows for processing search results.
- Living mode: manage monthly searches, identify and remove duplicates, apply any technology enablers, prepare search results for the author team, maintain accurate search records, update PRISMA flow diagram.
- Annual review: reassess the appropriateness of the search methods (sources, search terms, frequency) and ensure any amendments to the scope of the review are reflected in the search.

6.1 Starting out

6.1.1 Search methods for a new LSR protocol and baseline review

When embarking on a new LSR, the search methods (including sources, search strategies, frequency of searches, use of technological enablers, ongoing assessment and evaluation) should be described in detail in the protocol and in the baseline version of the review.

The author team will need to decide when to start the monthly searches. For reviews with relatively few studies and manageable search yields, teams may decide to enter living mode from the outset (i.e. commence monthly searches from the time when the baseline searches are run) and process monthly search results while the baseline version of the review is being produced and published. For larger reviews it may be more practical to complete and publish the baseline review first and then transition to living mode. In the latter case, the first update following publication of the baseline review will require the most effort in terms of screening and processing the backlog of search results.

6.1.2 Search methods when transitioning an existing review to an LSR

When transitioning an existing Cochrane Review to living mode, the search methods should be described in both the main text of the review and the LSR-specific methods appendix. At the time of transitioning to living mode, teams should assess if the search methods are still appropriate and revise to ensure ongoing searches perform well and search results are managed efficiently. This assessment should include consideration of sources, search terms and the use of enablers to process search results (see section '6.4: Assessing and refining search methods'). Peer review of the primary database strategy by an information specialist working within the same Cochrane network is highly recommended.

Evaluating the search methods when converting a review to living mode will also involve assessing the feasibility and usefulness of incorporating technology enablers to process the monthly search results. For reviews of randomised trials, the RCT classifier may reduce the number of records to screen by around 30% but depending on the monthly yield, you may decide that the time spent processing records through the classifier offers only marginal gains in efficiency. For reviews that generate a more substantial yield each month (~100 records or more) then use of the RCT classifier is worth considering.

Further guidance on revising and reporting search strategies when updating an existing review is provided in the Methodological Expectations of Cochrane Intervention Reviews (MECIR) standards (2) and Chapter IV of the Cochrane Handbook (25).

6.2 Ongoing evidence surveillance

As a minimum, living systematic reviews require monthly searching of key databases and trial registries. Any new version of the LSR published in the *CDSR* must comply with the following mandatory MECIR standards:

- search of CENTRAL, MEDLINE and Embase (Standard C24)
- search of ClinicalTrials.gov and WHO ICTRP (Standard C27)
- reference checking of any new included studies (Standard C30)

Searching other sources (e.g. regulatory agency websites, handsearching journals) or conducting supplementary searches (e.g. citation tracking) can be undertaken less frequently, for example every three or six months. The frequency of searching other sources will depend on literature dissemination activities in a given research area (e.g. availability of proceedings from key conferences), but should ideally always be up to date whenever a new version of the LSR is published.

Information about the frequency and range of searches that comprise the evidence surveillance approach must be clearly described in the protocol, and reported in the baseline review and subsequent updates.

Box 4: Monthly searches

Currently all Cochrane living systematic reviews conduct monthly searching and screening. There is ongoing discussion about the minimal search frequency for a review to be designated 'living', and whether it might be possible to vary this depending on the review question. The results of these conversations will be used to inform future revisions of this guidance.

Establishing standard processes for managing the monthly and other ongoing searches will increase the feasibility and sustainability of the LSR approach. Standard processes include:

- running monthly saved searches or setting up database auto-alerts, ideally all running on the same day or date each month
- removing duplicates, both from among the batch of new records as well as from records that have already been screened
- integrating the use of enablers, such as the RCT classifier or Cochrane Crowd
- preparing records to send to the author team (e.g. via email, Covidence or EndNote)
- maintaining an EndNote library (or equivalent) that captures all the search results over the lifetime of the review
- keeping accurate records of each new search (sources, dates, numbers of records, etc.)
 and what decision is made for each record screened.
 - This latter point is essential for accurate reporting of the search methods in the review, including the PRISMA flow diagram.

Box 5: Database searches

There are three main approaches to generating monthly search results from databases:

- 1. setting up auto-alerts in each database (if that functionality exists) and receiving notification via email on a set day each month
- 2. manually re-running saved searches using appropriate date limiters to retrieve only those records added to the database since the previous search
- 3. manually re-running saved searches across the entire database, retrieving all records and deduplicating against all previous yields.

Regardless of the approach used, duplicates should be removed from the combined monthly search yield and then further deduplicated against the cumulative search yield for the review, before providing the search results to the author team.

The distribution of tasks and coordination of the search workload should be determined at the outset. Typically, the information specialist will oversee the monthly searches and the authors the less frequent supplementary searches (e.g. cited/citing references, handsearching, contacting study authors, regulatory websites, etc.).

6.3 Reporting the search results

Whenever a new version of the LSR is published, the search results must be updated in the abstract, main body of the review and the PRISMA diagram. In addition, the What's New table Description field can be used to indicate the most recent search date and the status of processing the results of the search. See section '4.4: Informing readers about the currency of living systematic reviews' for further information on using the What's New table.

6.4 Assessing and refining search methods

Author teams, wherever possible, should include an information specialist who works with other team members to review the search methods annually, or sooner if changes occur in the research field that may impact the search methods. This will include consideration of new search terms and sources, and possible changes to the frequency of the supplementary searches. Teams could consider scheduling the review of search methods to coincide with the announcement each November/December by the National Library of Medicine of changes to the MeSH vocabulary.

Looking at the studies included in the review can determine the contribution of different sources (indicating which might be discontinued), as well as help identify search terms that add noise to the search, adversely impacting on the performance of the search strategy. This is also the time to make sure any changes to the scope of the review (i.e. PICO components) are reflected in the inclusion of appropriate thesaurus (e.g. MeSH) and free-text terms, and that the original search is current with respect to any new thesaurus terms or changes to database search syntax.

Note that substantial changes to the review, especially an expansion of scope, may require searches to be re-executed across the entire period covered by the original searches.

Other aspects of managing search results (e.g. whether to use technology enablers) should also be reviewed at this time.

7 Authorship and living systematic reviews

Standard Cochrane authorship considerations apply to Cochrane LSRs (49), and LSRs also present unique challenges to managing authorship. For example, the evaluation of Cochrane pilot LSRs found that due to the quick turnaround required and number of contributors available, some authors on earlier versions of the LSR were either unavailable to contribute to core review tasks for subsequent updates, or there was very little review work to be done. For many LSRs, it is likely that the relative contributions of authors will vary across versions of an LSR. Therefore, it is expected that the author team will evolve over time.

It is strongly recommended that LSR teams discuss authorship management as early as possible. Teams wishing to explore an approach that is not documented in the Cochrane authorship policy can contact the <u>EMD</u> Publishing team.

It is important that authors understand how the current versioning functionality applied within the *CDSR* is related to publication metrics, such as number of citations per publication. At the time of finalising this guidance, each update of an LSR is regarded as an individual publication and has a unique DOI. While this results in an increased number of publications for authors, the number of citations for an LSR is spread across all versions, thereby reducing the number of citations per individual publication. In the future, it may be possible to group all versions of an LSR using mechanisms such as linked DOIs, to produce a metric that accumulates citations across all versions of an LSR.

8 Transitioning a living systematic review out of living mode

8.1 When to transition a living systematic review out of living mode

Just as the decision to commence a living systematic review requires careful consideration, deciding to cease maintaining a review in living mode also requires consideration and prespecification.

It is likely that ongoing continual updating of some LSRs will eventually become inappropriate. The reasons for an LSR to be transitioned out of living mode should be predetermined and specified in the protocol.

For example, the review question may no longer meet all three criteria listed above in section '3.1 When is a living systematic review worth doing?' That is:

- the research question is no longer a priority for decision-making (e.g. the intervention may have been superseded or withdrawn).
- a reasonable level of certainty has been reached in the existing evidence.
- research that might impact the conclusions of the review is no longer emerging (e.g. the research area is no longer active).

It is recommended that LSR teams assess the appropriateness of continuing to maintain the LSR on an annual basis. Alternatively, Cochrane Review Groups may want to consider whether a given LSR should continue to be maintained as part of priority setting activities. Factors that could be examined include article-level metrics (e.g. Altmetrics; downloads; citations); knowledge translation activities arising from an LSR, including impact on policy and practice; and new research initiated (50).

In addition, a range of practical factors may influence whether an LSR continues to be maintained. These include whether the necessary resources (e.g., funding, author and editorial team capacity) remain available.

Note: Similar to the decision to initiate an LSR, the decision to transition an LSR out of living mode rests with the editorial team.

Ideally, the author team will make a pre-planned transition out of living mode. That is, one final update is undertaken to include any new evidence found since the last update and modify/remove text regarding LSR methods. A process for this is described below. When resources are not available to transition the LSR out of living mode using the process described below, LSR teams can contact the <u>LSR support team</u> for advice.

8.2 Process for transitioning a living systematic review out of living mode

A central aim of the process for transitioning an LSR out of living mode is to inform the reader that the systematic review is no longer in living mode. Teams can follow the steps below, once the decision has been made to transition an LSR out of living mode.

The following sections of the Cochrane Review will need to be modified:

- Abstract, Plain Language Summary and Background: Modify these to indicate:
 - that the review was previously an LSR
 - o the timeframe for which the review was an LSR
 - why the review was transitioned out of living mode

Background:

- o Remove text about the rationale for an LSR approach from the sub-section Why it is important to do this review
- o If applicable, remove the secondary objective of maintaining the review as an LSR.
- Methods: Search methods for identification of studies:
 - Remove text about ongoing evidence surveillance (e.g. monthly database and clinical trial registries searches; conference abstracts) from the <u>Electronic sources</u> and <u>Searching other resources</u> sub-sections.
- Selection of studies: Remove text about screening the ongoing searches.
- <u>Data synthesis:</u> Remove LSR-specific text (e.g. immediately extracting and analysing data after screening the monthly searches).
- Methods for future updates:
 - o Remove LSR-specific text about reviewing the methods.
 - Remove text about the conditions under which the review will no longer be maintained as an LSR.
- Differences between protocol and review:
 - For an LSR that was transitioned from a standard Cochrane Review to an LSR, this section can be adjusted to reflect the transition back to a standard review.
 - For an LSR that commenced as a new review following publication of an LSR protocol, this section will need to be modified to reflect that the review has been transitioned out of living mode.

• Appendices:

- For an LSR that was transitioned from a standard Cochrane Review to an LSR, the LSR-specific methods appendix can be removed. (For readers wanting to access the LSR methods, a link can be provided to the most recent version of the review that included these methods).
- Authors can search the review text for any remaining LSR-related terms (e.g. "living" or "LSR" or "LNMA") to identify other aspects of the review text that may need to be modified or removed, as appropriate.

Once the update has been produced and published, the Managing Editor can update the What's New field according to standard Cochrane policy; see https://documentation.cochrane.org/pages/viewpage.action?pageId=117380266.

Notes:

- 1. Some prior LSRs may be updated in future as per the standard update process for Cochrane Reviews.
- 2. Teams may choose to suspend automated evidence surveillance methods (e.g. bibliographic database auto-alerts).
- 3. At the time of finalising this version of the guidance, no Cochrane LSRs had been transitioned out of living mode. Accordingly, the process outlined above may evolve over time. Teams who have decided to transition an LSR out of living mode are encouraged to contact the <u>LSR support team</u> for assistance with the process.

9 Resources for LSR teams

9.1 Cochrane's living systematic reviews website

The Cochrane living systematic reviews website provides links to a range of resources including

- LSR series in Journal of Clinical Epidemiology
- List of Cochrane's published LSRs
- Report on Cochrane's evaluation of pilot LSRs
- Cochrane Learning Live webinar introducing LSRs
- LSR library on Mendeley
- <u>Living Evidence Network webinars.</u> Examples include:
 - LSR searching
 - o technological enablers for living evidence
 - o living network meta-analysis

9.2 Living Evidence Network

The Living Evidence Network (LEN) is facilitated by Cochrane. Initially named the Living Systematic Review Network, it commenced in early 2016 to bring together those involved in Cochrane's first LSR pilots. The Network now includes over 270 systematic review and guideline development researchers and practitioners, within and outside Cochrane, who are planning or undertaking living evidence projects such as LSRs or living guidelines, or are interested in certain aspects (e.g. technological enablers).

The purpose of the LEN is to

- share ideas, information and resources
- further the thinking on the living evidence concept and methods

The LEN includes 5 interest groups:

- Search
- Technology
- Methods
- Publication
- Knowledge Translation and Stakeholder Engagement

More information about the LEN can be found in the <u>governance structure</u>, including the roles of the Steering Group, Interest Group Co-Leads and working groups.

If you would like to join the Living Evidence Network and be kept up to date about LEN activities, including upcoming webinars, please email lsr@cochrane.org

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11 Appendix 1. List of contributors

Many members of the Living Evidence Network contributed to the conceptualisation of LSRs that informed this document, or provided verbal or written feedback on document drafts. Living Evidence Network members as at 11 October 2019 include:

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12 Appendix 2: Cochrane LSR protocol and LSR templates

Column 1 of the table below highlights LSR-specific considerations for preparing a living systematic review protocol or producing a living systematic review. Column 2 provides suggested text and examples for an LSR protocol, while Column 3 provides the same for an LSR. These templates are intended to supplement, not replace guidance provided in the MECIR standards (2) and Cochrane Handbook.

Methods considerations specific to LSRs	LSR protocol suggested text and/or examples	LSR suggested text and/or examples
Title		
	The title for an LSR does not indicate that the review is live the review title must be appropriate for a standard Cochi	ving. Given that an LSR may transition out of living mode, rane Review.
What's New		
The What's New table is used to provide monthly updates regarding the currency of the LSR.	Section not applicable to protocol	For information and examples relating to using the What's New table for LSRs, please refer to section '4.4 Informing readers about the currency of living systematic reviews' in the main text of this guidance.
History		
	Section not applicable to protocol	For information about the History section, please refer to section '4.4 Informing readers about the currency of living systematic reviews' in the main text of this guidance.
Abstract		
At the end of the abstract, i.e. the end of the Authors conclusions section, provide the standard editorial text to identify the review as an LSR.	Section not applicable to protocol	Suggested text Editorial note: This is a living systematic review. We search for new evidence every month and update the review when we identify relevant new evidence. Please

Methods considerations specific to LSRs	LSR protocol suggested text and/or examples	LSR suggested text and/or examples
		refer to the Cochrane Database of Systematic Reviews for the current status of this review.
Plain language summary		
At the end of the plain language summary, provide the standard editorial text to identify the review as an LSR.	Section not applicable to protocol	Editorial note: This is a living systematic review. We search for new evidence every month and update the review when we identify relevant new evidence. Please refer to the Cochrane Database of Systematic Reviews for the current status of this review.
Background		
Description of the condition; Description of the interv	rention; How the intervention might work	
No changes proposed	N/A	N/A
Why it is important to do this review		
It should be clear to the reader why an LSR approach is appropriate for your Cochrane Review. LSRs build on recent guidance (24) about when a systematic review update is appropriate.	No suggested text is provided, given this will vary from review to review.	No suggested text is provided, given this will vary from review to review.
Broadly speaking, an LSR may be appropriate when all three of the following criteria are met: • The review addresses a particularly important	Example 1"This topic lends itself to a living systematic review approach for several reasons. First, knee osteoarthritis	<u>Example 1</u>"We believe a living systematic review approach is appropriate for this review for four reasons. First, the
 The review addresses a particularly important question for practice or policy (now or likely in the near future) There is an important level of uncertainty in 	is a condition for which there is a high demand for new therapies, due to its prevalence, impact on function and quality of life, and paucity of highly effective	review addresses an important topic for clinical practice; patients with cancer have a relatively high rate of VTE, up to 17.7% (Ay 2010). In addition, the

Methods considerations specific to LSRs LSR protocol suggested text and/or examples LSR suggested text and/or examples the existing evidence nonsurgical treatments. This has led to a occurrence of VTE is associated with a 2.3 increased There is (likely to be) emerging evidence (e.g. commensurate increase in the supply of treatment risk of death in patients with breast and non-small cell in trial registries) that will impact on the options, many of which have been instituted into lung cancer (NSCLC), 2.5 times lengthening of hospital conclusions. practice before a robust evidence base for their stay among patients with lung cancer, and 50% higher total cost for patients with lung cancer (Chew 2008, effectiveness has been established. Nonpharmacological therapies, including autologous Chew 2007; Connolly 2012). Second, there remains blood product injections, have been well placed to fill uncertainty in the existing evidence base; the 2014 this gap in the market as they are subject to fewer update of this systematic review found a potential regulatory restrictions than pharmaceutical products. subgroup effect on all-cause mortality at one year, with PRP injections are now widely used for a variety of a possible higher reduction in mortality among indications, particularly osteoarthritis and other patients with small cell lung cancer (SCLC) compared disorders of the knee (Zhang 2016), despite relatively to other types of cancer. Third, we are aware of several little high-quality evidence to date. Second, the use of recently published and ongoing trials in this area that PRP and other autologous blood products for the will be important to incorporate in a timely manner." treatment of osteoarthritis is an active area of research, (adapted from 10) with several trials currently in progress. It is likely that the conclusions of this review, including estimates of the efficacy of the interventions, will change as new evidence is added in the near future. Finally, due to the large burden of disease attributable to knee osteoarthritis, it is important that consumers, healthcare providers and policy-makers have the most up-to-date summary of the evidence for this intervention, in order to make informed decisions" (18). **Objectives** It is appropriate, and likely to be helpful for the reader, Suggested text Suggested text to make the fact that this review will be updated using an LSR approach explicit in the objectives. Rather than "A secondary objective is to maintain the currency of "A secondary objective is to maintain the currency of altering the main objective(s), this can be added as a the evidence, using a living systematic review the evidence, using a living systematic review second, or subsequent, objective. approach." approach."

Methods considerations specific to LSRs	LSR protocol suggested text and/or examples	LSR suggested text and/or examples
Methods: Criteria for including studies in the review		
Types of studies, Types of participants, Types of interventions, Types of outcome measures		
No changes proposed	N/A	N/A
Methods: Search methods for identification of studies		

Electronic sources

With living systematic reviews, we are particularly interested in keeping abreast of emerging and ongoing study findings, in addition to existing published study reports. As such, as much as possible, all search sources should be searched at frequent and regular periods (i.e. monthly for the main bibliographic databases and clinical trial registries). Search frequency for all sources must be stated in the protocol.

To be concordant with Cochrane standards, there should be no changes to standard Cochrane guidance around search methods. This means scoping or top-up searches are not sufficient. As such, searches of all electronic databases, clinical trial registries, and potentially other sources that will identify trials in progress, need to be run each time the search is conducted.

Search strategies also need to be reviewed over time as indexing terms (e.g. MeSH) and keywords can change, and new search filters may be published. You may also

Suggested heading

Living systematic review considerations

[NEW Level 3 heading at end of this section]

No suggested text is provided, given this will vary from review to review.

Example 1

"As a living systematic review, the majority of searches will be re-run monthly. For the electronic databases and other electronic sources (including clinical trials registries), we will set up auto-alerts (where possible) to deliver a monthly search yield by email."

"Search methods and strategies will be reviewed approximately yearly, to ensure they reflect any terminology changes in the topic area, or in the databases."

Suggested heading

Living systematic review considerations

[NEW Level 3 heading at end of this section]

No suggested text is provided, given this will vary from review to review.

Example 1

"Living review approach: The last major search was in February 2016. We have been running monthly searches since then. We will incorporate new evidence rapidly after it is identified. This review update is based on the findings of a literature search conducted on 14 August 2017. We will reconsider search methods and strategies once a year to ensure they reflect any terminology changes in the topic area, or in the databases". (10)

Methods considerations specific to LSRs	LSR protocol suggested text and/or examples	LSR suggested text and/or examples
find some of your search sources are redundant, or other sources should be added. This will be topic-dependant and should be decided in consultation with the Review Group. Your plan to manage this should be described. (NOTE: This may change with Cochrane system developments such as the Evidence Pipeline and Cochrane Crowd). For further information on LSR searching methods, see section '6: Managing searches for living systematic reviews' in the main text of this guidance.	"Database searches will be run monthly from the date of the baseline review search. Any studies identified in the period from the baseline searches to publication of the review will either be incorporated in the review or noted in the 'What's new' section and included in the first update. For the searches of CENTRAL, MEDLINE and Embase, we will use auto-alerts in the Cochrane Library and Ovid to receive a monthly search yield by email. We will also manually search ClinicalTrials.gov and the WHOICTRP trials portal. We will review search methods (sources, search terms and frequency) approximately yearly to ensure they reflect any changes in subject headings or textwords, as well as any changes in the eligibility criteria of the review." (19)	
Searching other resources		
Searching additional sources may need to be undertaken at the same frequency as database or	Suggested heading	Suggested heading
electronic sources. For some 'Other sources' such as websites or conference proceedings, less frequent searching may be appropriate (but no less frequently	Living systematic review considerations [NEW Level 3 heading at end of this section]	Living systematic review considerations [NEW Level 3 heading at end of this section]
than yearly). This should be clearly described in the protocol.	No suggested text is provided, given this will vary from review to review.	No suggested text is provided, given this will vary from review to review.
	Example 1	Example 1
	"In developing this living systematic review, we will note when these key conferences are to be held and will search conference proceedings when published. We will contact corresponding authors of ongoing	"We are searching other resources (articles published in three relevant international peer reviewed journals: Journal of Nutrition Education and Behavior, Public Health Nutrition, and Journal of the Academy of

Methods considerations specific to LSRs	LSR protocol suggested text and/or examples	LSR suggested text and/or examples
	studies as we identify them and will ask them to advise when study results are available, or to share early or unpublished data. We will contact the corresponding authors of any newly included studies for advice regarding other relevant studies. We will manually search the reference lists of all newly included studies". (20)	Nutrition and Dietetics; database of published dissertations; and grey literature in Google Scholar) manually every six months. As additional steps to inform the living systematic review, we are contacting corresponding authors of ongoing studies as they are identified and asking them to advise when results are available, or to share early or unpublished data. We are contacting the corresponding authors of any newly-included studies for advice about other relevant studies. We are conducting citation tracking of included studies in Web of Science Core Collection on an ongoing basis. For that purpose, we have set up citation alerts in Web of Science Core Collection." (adapted from 8)
Methods: Data collection and analysis		
Selection of studies		
In an LSR, the searches must not only be run frequently, but the yield screened at the same frequency. (There is no point running monthly searches if they are only screened six-monthly). This must be stated in the protocol.	Suggested heading Living systematic review considerations [NEW Level 3 heading at end of this section]	Suggested heading Living systematic review considerations [NEW Level 3 heading at end of this section]
LSRs may use some of Cochrane's newer systematic review enablers (e.g. Screen4Me; the RCT Classifier; Cochrane Crowd) and technological enablers developed by other organisations (e.g. Systematic Review Accelerator). How technological enablers will	Suggested text to be included in a more detailed description: "We will immediately screen any new citations retrieved by the monthly searches." Example 1	Suggested text to be included in a more detailed description: "We will immediately screen any new citations retrieved by the monthly searches." Example 1

Methods considerations specific to LSRs	LSR protocol suggested text and/or examples	LSR suggested text and/or examples
be used in your LSR should be made explicit. See section ' <u>5: Living systematic review enablers</u> ' for information about technological enablers.	"We will immediately screen any new citations retrieved by the monthly searches. We expect initial search yields to be fairly small, so we intend to screen all records manually without applying the RCT classifier, however, this or other automation techniques may be employed over time if the volume of retrieved citations increases substantially." (adapted from 19)	"We will immediately screen any new citations retrieved by the monthly searches. As the first step of monthly screening, we will apply the machine learning classifier (RCT model) (51) available in the Cochrane Register of Studies (CRS-Web). The classifier assigns a probability (from 0 to 100) to each citation of being a true RCT. For citations that are assigned a probability score below the cut-point at a recall of 99% we will assume these to be non-RCTs. For those that score on or above the cut-point we will either manually dual screen these results or send them to Cochrane Crowd for screening." (adapted from 8)
Data extraction and management, Assessment of risk	of bias of included studies	
No changes proposed	N/A	N/A
Measures of treatment effect, Unit of analysis issues,	Dealing with missing data	
No changes proposed	N/A	N/A
Assessment of heterogeneity, Assessment of reportin	g biases	1
No changes proposed	N/A	N/A
Data synthesis		

Methods considerations specific to LSRs

Deciding when to incorporate new evidence

During the life of an LSR, it is expected that review teams will identify not only new studies, but other potentially important data and information relevant to the review and its already included studies. For example, new outcome or adverse events data may become available for an existing (included) trial, an ongoing trial may cease, a now completed trial may remain unpublished, or a study publication may be retracted.

Given that LSRs are only likely to be undertaken on topics for which new evidence is likely to have an important impact on the review conclusions, the default position should be that new studies and any important new data or information should be immediately incorporated into the review. However, there may be instances where the new studies, data or information do not sufficiently change the findings or credibility of the review to warrant immediate inclusion. In these instances, the authors may choose to wait until the next time this threshold is reached before incorporating this new information into the review.

LSR teams can flag the existence of unincorporated new information to the reader using the What's New table.

Authors should pre-specify how they will decide whether newly identified studies, data or information will not be immediately incorporated into the review. Guidance for making this decision is available in Garner

LSR protocol suggested text and/or examples

Suggested heading

Living systematic review considerations

[NEW Level 3 heading at end of this section]

<u>Deciding when to incorporate new evidence</u>

No suggested text is provided, given this will vary from review to review.

Example 1:

Whenever new evidence (meaning studies, data or other information) relevant to the review is identified, we will extract the data and assess risk of bias, as appropriate. We will immediately incorporate any new evidence into the review.

Example 2:

Whenever new evidence (meaning studies, data or other information) relevant to the review is identified, we will extract the data and assess risk of bias, as appropriate. We will wait until the accumulating evidence changes one or more of the following components of the review before incorporating it and re-publishing the review:

- The findings of one or more primary outcomes
- The credibility (e.g. GRADE rating) of one or more primary outcomes
- New settings, populations, interventions, comparisons or outcomes studied

LSR suggested text and/or examples

Suggested heading

Living systematic review considerations

[NEW Level 3 heading at end of this section]

Deciding when to incorporate new evidence

No specific text is suggested, given this will vary from review to review.

Example 1:

"Whenever we find new evidence (i.e. studies, data or information) meeting the review inclusion criteria, we will extract the data, assess risk of bias and incorporate it in the synthesis every four months, as appropriate. We will incorporate any new study data into existing meta-analyses using the standard approaches outlined in the Data synthesis section". (adapted from 8)

Methods considerations specific to LSRs	LSR protocol suggested text and/or examples	LSR suggested text and/or examples
(24; see Step 3: assess the effect of updating the review) and Chapter 22 of the Cochrane Handbook (26). Also see <u>Box 2</u> in the main text of this guidance.	New serious adverse eventsOther [author teams to specify]	
As an alternative to immediately updating the LSR when new evidence that has an important impact on the review conclusions is identified, a decision may be made to update the LSR on a fixed-interval schedule when a high volume of new evidence is anticipated. As an example, the Cochrane pilot LSR with the highest rate of new evidence was updated every 4 months during the pilot period (8). Making this decision can be helped by checking trial registries and, if the review has been published before, checking how many studies were found in the last few years. Teams choosing this alternative need to consider what actions will be taken for the following two scenarios and pre-specify these in the protocol:		
 A scheduled update is due to be undertaken, but the ongoing searches have identified no new evidence. A scheduled update is due to be undertaken, and the ongoing searches have only identified new evidence that is unlikely to change the review conclusions. 		
Adjustments for repeated meta-analyses	Adjustments for repeated meta-analyses	Adjustments for repeated meta-analyses
Sequential methods should not be used for the main analyses in an LSR or to draw main conclusions. Further information about the rationale for not applying error-adjustment techniques for repeated meta-analyses can be found in Chapter 22 of the	It is optional to make an explicit statement about error adjustment techniques. Authors may wish to clarify that such techniques will not be applied to Cochrane LSRs.	It is optional to make an explicit statement about error adjustment techniques. Authors may wish to clarify that such techniques will not be applied to Cochrane LSRs.

Methods considerations specific to LSRs	LSR protocol suggested text and/or examples	LSR suggested text and/or examples
Cochrane Handbook (26).	Suggested text:	Suggested text for a baseline review for a new LSR:
	"Formal sequential meta-analysis approaches will not be used for updated meta-analyses".	"Formal sequential meta-analysis approaches will not be used for updated meta-analyses".
		Suggested text for an updated review: "Formal sequential meta-analysis approaches were not applied to the updated meta-analyses".
Subgroup analysis and investigation of heterogeneity	, Sensitivity analysis, Summary of Findings Table	
No changes proposed	N/A	N/A
Methods for future updates [This is an optional heading	g in RevMan, which can be activated for LSRs]	
When review methods will be reviewed In an LSR approach, authors will not necessarily have	Suggested heading Living systematic review considerations	Suggested heading Living systematic review considerations
the same trigger to review the methods for any necessary revisions, in the same way that they	[NEW Level 3 heading at end of this section]	[NEW Level 3 heading at end of this section]
currently do with standard review updates. Authors should pre-specify when they will review the methods.	When review methods will be reviewed Suggested text: We will review the review scope and methods approximately yearly, or more frequently if appropriate, in light of potential changes in the topic area or the evidence being included in the review (for example, additional comparisons, interventions, sub- groups or outcomes, or new review methods available).	When review methods will be reviewed Suggested text: We will review the review scope and methods approximately yearly, or more frequently if appropriate, in light of potential changes in the topic area or the evidence being included in the review (for example, additional comparisons, interventions, sub- groups or outcomes, or new review methods available).
The conditions under which the review will no longer be maintained as an LSR	The conditions under which the review will no longer be maintained as an LSR	The conditions under which the review will no longer be maintained as an LSR
It is anticipated that reviews may cease to need to be living over time, as the review findings become stable,	No suggested text is provided, given this will vary from review to review.	No suggested text is provided, given this will vary from review to review.

Methods considerations specific to LSRs	LSR protocol suggested text and/or examples	LSR suggested text and/or examples
the credibility improves (e.g. evidence quality becomes high) or the question is no longer a priority for decision-makers. Authors are encouraged to put some thought into possible scenarios under which they envisage the review may no longer need to be maintained as an LSR, acknowledging it is difficult to predict all future possible scenarios. For information on the process to transition an LSR out of living mode, see section '8: Transitioning a living systematic review out of living mode'.	Example 1 "We will consider each year the necessity for the review to be living by assessing ongoing relevance of the question to decision-makers and by determining whether uncertainty is ongoing in the evidence and whether further relevant research is likely". (20)	Example 1 "We will make decisions about whether to stop updating when appropriate (e.g. if conclusions are unlikely to change with future updates; no meaningful effect is likely to be found; the review question is no longer a priority for decision-making; or no new evidence is likely), and will be guided by ongoing work in this area (Elliott 2017)." (19)
Results		
No changes proposed	Section not applicable to protocol	N/A
Discussion		
Summary of main results		
No changes proposed	Section not applicable to protocol	N/A
Quality of the evidence, Potential biases in the review	process, Agreements and disagreements with other stu	udies or reviews
No changes proposed	Section not applicable to protocol	N/A
Authors' conclusions		
No changes proposed	Section not applicable to protocol	N/A
Differences between protocol and review		
For an existing Cochrane Review that is being	Section not applicable to protocol	Suggested text

Methods considerations specific to LSRs	LSR protocol suggested text and/or examples	LSR suggested text and/or examples
transitioned to an LSR, the <i>CDSR</i> function to publish a new protocol is not yet available. Therefore, in this section authors should note that the updated review includes additional methods pertaining to the LSR and refer the reader to the living systematic review protocol appendix.		This update includes some new methods relevant to living systematic reviews, which are described in the Methods and Appendix 1 (Living systematic review protocol).
Appendices		
For an existing Cochrane Review that is being transitioned to an LSR, the <i>CDSR</i> function to publish a new protocol is not yet available. In the interim, an LSR-specific methods appendix to the published LSR serves as a substitute for publishing a new protocol. Note: This approach may change when the functionality to publish a new protocol for existing reviews becomes available in the <i>CDSR</i> .	N/A	The information below is only applicable to an existing Cochrane Review that is being transitioned into living mode. The example appendix below is intended to demonstrate the relevant sub-headings to include. The text under each sub-heading will vary across LSRs according to the specific method decisions made by the author team about search methods and data synthesis. Suggested appendix title: Living systematic review protocol Appendix text example 1 (adapted from 8)
		The methods outlined below are specific to maintaining the review as a living systematic review on the CDSR. Core review methods, such as the criteria for considering studies in the review and assessment of risk of bias, are unchanged. As such, below we outline only those areas of the Methods for which additional activities or rules apply. Search methods for identification of studies We will re-run electronic database and trial registry
		searches monthly. For the electronic databases

Methods considerations specific to LSRs	LSR protocol suggested text and/or examples	LSR suggested text and/or examples
		(CENTRAL, Epub Ahead of Print, In-Process & Other
		Non-Indexed Citations, MEDLINE Daily and MEDLINE
		and Embase) and other electronic sources (WHO
		International Clinical Trials Registry Platform and
		clinicaltrials.gov), we will set up auto-alerts (where
		possible) to deliver a monthly search yield by email.
		We will search other resources (articles published in
		three relevant international peer reviewed journals:
		Journal of Nutrition Education and Behavior, Public
		Health Nutrition, and Journal of the Academy of
		Nutrition and Dietetics, database of published
		dissertations; and grey literature in Google Scholar)
		manually every six months.
		As additional steps to inform the living systematic
		review, we will contact corresponding authors of
		ongoing studies as they are identified and ask them to
		advise when results are available, or to share early or
		unpublished data. We will contact the corresponding
		authors of any newly-included studies for advice about
		other relevant studies. We will conduct citation
		tracking of included studies in Web of Science Core
		Collection on an ongoing basis. For that purpose, we
		have set up citation alerts in Web of Science Core
		Collection. We will manually screen the reference list of
		any newly-included studies and systematic reviews.
		Also, we will use the 'related citation' feature in
		PubMed to identify additional articles. We will review
		search methods and strategies approximately yearly,
		to ensure they reflect any terminology changes in the
		topic area, or in the databases.

Methods considerations specific to LSRs	LSR protocol suggested text and/or examples	LSR suggested text and/or examples
		Selection of studies
		We will immediately screen any new citations retrieved
		by the monthly searches. As the first step of monthly
		screening, we will apply the machine learning classifier
		(RCT model) (51) available in the Cochrane Register of
		Studies (CRS-Web). The classifier assigns a probability
		(from 0 to 100) to each citation for being a true
		randomised controlled trial (RCT). For citations that are
		assigned a probability score below the cut-point at a
		recall of 99% we will assume these to be non-RCTs. For
		those that score on or above the cut-point we will
		either manually dual screen these results or send them
		to Cochrane Crowd for screening.
		Data synthesis
		Whenever we find new evidence (i.e. studies, data or
		information) meeting the review inclusion criteria, we
		will extract the data, assess risk of bias and incorporate
		it in the synthesis every four months, as appropriate.
		We will incorporate any new study data into existing
		meta-analyses using the standard approaches outlined
		in the Data synthesis section. Error-adjustment
		methods will not be applied to repeated meta-
		analyses.
		Other
		At least annually, we will consider the review scope and
		methods in light of potential changes in the topic area,
		or the evidence being included in the review (e.g.
		additional comparisons, interventions or outcomes, or
		new review methods available).