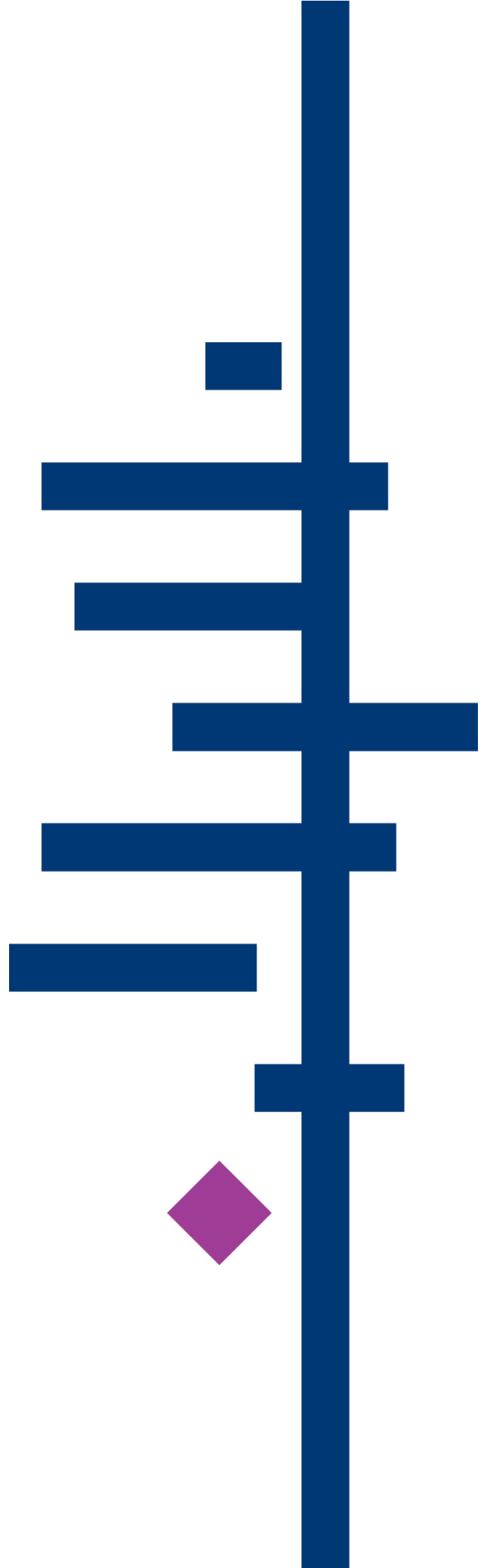**Project Transform**

Cochrane Living Systematic Reviews

Interim guidance for pilots
(Version 0.3, 21 April 2017)

**Trusted evidence.
Informed decisions.
Better health.**

Contents

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Purpose

The purpose of this document is to outline the methods and production and publication models for *pilot* Living Systematic Reviews (LSRs) published on The Cochrane Library. It includes a protocol template for a Cochrane LSR (see Appendix 2).

This document is primarily designed to be a practical guidance document for the authors, Review Groups and Central Editorial Unit staff involved in the first round of Cochrane LSR pilots.

The approach described here is based on our review of current literature relevant to living systematic reviews and consultation with a range of stakeholders, including the Living Systematic Review Network, which includes members within Cochrane and beyond (see Appendix 1). The approach outlined is a work in progress. The ideas presented will be evaluated and refined on the basis of the pilot Reviews.

In addition, the new evidence ecosystem is evolving quickly, and the opportunities and implications for the production and publication of LSRs will continue to develop over time.

Introduction

Why Living Systematic Reviews are 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 reliable; meaning both that the methods they employ must be trustworthy, and reviews must reflect all of the results of relevant research, including the most recently published data.

Cochrane Reviews and the methods they employ are acknowledged to be rigorous, however this has often come at the cost of currency. Cochrane Reviews frequently 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.

Cochrane authors are now encouraged to make more explicit decisions about when to update their reviews. The Updating Classification System (1), provides a decision framework informed by the value of incorporating any known new studies, data, information or methods to the review. 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 continuous updating model.

Living Systematic Reviews (LSRs), in alignment with Cochrane's updating guidance, provide a new approach to the ongoing efforts of Cochrane and others to provide evidence on these 'hot topics' that is both trustworthy and current. While similar to frequently updated 'conventional' Cochrane Reviews, LSRs aim at the outset to achieve a high degree of currency by continuous monitoring of the evidence and require authors to make explicit commitments as to the frequency and methods of updating.

The concept of living evidence synthesis and related outputs, such as living guidelines, are of increasing interest to evidence producers, decision makers, guideline developers, funders and publishers, as a way to seamlessly connect evidence and practice.

The possibility of a scaled-up living evidence approach has only recently been within reach, due to a number of technological and data-related innovations, such as online platforms, linked data, and machine learning. Concurrently, research groups are embracing larger collaborations, open and shared data, and the growth of the citizen science movement, opening up the possibility of communities with a common interest maintaining high value datasets and associated Living Systematic Reviews.

Why Cochrane is piloting Living Systematic Reviews?

The original vision for Cochrane was that it would "include a library of trial overviews, which will be updated when new data become available" (2) (p.287). Cochrane has led the way in systematic review conduct, and has always been committed to updating reviews, however achieving the vision of continuously maintaining the currency of Cochrane Reviews has proven impossible in practice. By harnessing new review production approaches and technologies, Living Systematic Reviews provide an opportunity to make the vision of Cochrane co-founder Ian Chalmers a reality for selected reviews.

What is a living systematic review?

Definition of a Living Systematic Review

We define an LSR as a systematic review which is continually updated, incorporating relevant new evidence as it becomes available (adapted from (3)).

Practically, this means that LSRs:

- Are underpinned by continual, active monitoring of the evidence (i.e. monthly searches)
- Immediately include any new important evidence (meaning data, studies or information) that is identified
- Are supported by up-to-date communication about the status of the review, and any new evidence being incorporated

While core review methods are not fundamentally different to other Cochrane Reviews, an LSR should additionally include explicit, transparent and predefined decisions on:

- How frequently new evidence is sought and screened
- When and how new evidence is incorporated into the review

More detail about what should be pre-specified in an LSR protocol is provided in Appendix 2.

How a Living Systematic Review differs from other types of reviews

Table 1 (below) outlines the key differences between LSRs and other approaches to maintaining review currency, including reviews that are frequently updated, rapid reviews and standard systematic reviews.

TABLE 1. COMPARISON OF KEY FEATURES OF LSRS WITH OTHER SYSTEMATIC REVIEW TYPES

	Living Systematic Review	Frequently updated review	Rapid Review	Standard Systematic Review
Explicit, pre-defined methods describing search frequency	✓	✗	✗	✗
Explicit, pre-defined methods describing when and how new evidence is incorporated into the review	✓	✗	✗	✗
Continuous 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)	✓	✓	?	✓
Meta-analytic methods adjusted for frequent updating	?	?	✗	✗

When to do a Living Systematic Review

When a Living Systematic review is appropriate

Rather than being an automatic updating approach that is applied to all reviews in the Cochrane Library, authors and editorial teams should make an explicit and careful decision about the appropriateness of commencing an LSR. Equally, as a review topic becomes less of a priority, or the findings increasingly conclusive, it may no longer need to be maintained as an LSR.

The LSR method will be appropriate for some Cochrane Reviews for part of their life cycle.

Consideration of the conditions under which an LSR is appropriate has been informed by recent guidance on updating systematic reviews (4). According to this decision framework, the following three questions can be used to guide whether an update is appropriate:

1. Does the review address a current question?
2. Are there any new studies, or new information?
3. Will new studies, information, or data change findings or credibility?

For a sub-set of reviews, an LSR approach to updating may be appropriate.

We suggest an LSR is appropriate when all three of the following criteria are met:

1. The review question in a particular priority for decision making

With current review production and publication systems, LSRs are only appropriate when the question is of sufficient importance to health decision-making to make the allocation of the necessary resources worthwhile. Optimally, the importance of the question would also lead to the LSR being linked to living recommendations, policy statements or other approaches for translating the results of the review into practice and/or policy. In the future, as evidence surveillance and review updating becomes more efficient, an LSR approach may be appropriate for a broader range of questions.

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

A living systematic review is only likely to be useful where the current body of evidence does not provide an adequate basis for the answer to the review question to be considered certain and settled. Uncertainty of the evidence in systematic reviews is often informed by the GRADE assessment of the body of evidence underpinning each outcome. Review conclusions with a high level of certainty are those with the GRADE rating of 'high', and are not likely to change with the addition of new evidence. But uncertainty in the existing evidence may relate to an absence of good quality systematic reviews on the question of interest, gaps in the primary evidence, for example studies in particular populations or settings, or changes in the topic area, for example, new interventions being tested in primary studies.

3. There is likely to be emerging evidence that will impact on the conclusions

LSRs are appropriate when the research field covered by the review is moving relatively quickly and new evidence is being generated. The author team should have a good sense of the volume of research being undertaken in the immediate future, e.g., through examination of trial registries. It should also be likely that this evidence will influence policy and practice.

Methods for Living Systematic Reviews

Key points related to LSR methods are outlined below. More detailed methodological guidance is provided in the LSR protocol template (see Appendix 2).

Core review methods are largely unchanged

- Cochrane LSRs follow the same core methods, and review steps as standard Cochrane Reviews. What differs is that some additional a priori decisions about how the review will be maintained as an LSR.

An LSR must include ongoing evidence surveillance and be continually updated

- LSRs include active, ongoing evidence surveillance (i.e. monthly and include ongoing studies) and with updates provided to the reader when new studies, data, evidence or information is identified.

Additional decisions related to LSRs must be considered

- An LSR requires that there are explicit, transparent and predefined decisions about how frequently new evidence is sought and screened and when and how new evidence is incorporated into the review.

LSR decisions must be specified a priori

- There is an expectation that LSR-specific decisions are planned and reported in the relevant sections of the methods of the protocol.

New reviews and updates can be LSRs

- A Cochrane Review can be set up as an LSR at the outset, or an existing Cochrane Review can be transitioned into a Cochrane LSR.

LSRs build on a standard Cochrane Review

- Whether an author team is publishing a new review, or transitioning an existing review, there will need to be up-to-date 'baseline' review to build upon.

Any systematic review type can be an LSR

- While the guidance in this document has been developed with a standard Cochrane intervention review in mind, the concept can be applied to any review type.

Production and publication workflow

Key points related to producing and publishing Cochrane LSRs

New reviews and updates can be LSRs

- A Cochrane Review can be set up as an LSR at the outset, or an existing Cochrane Review can be transitioned into a Cochrane LSR.

LSR methods must be in included in protocols

- There is an expectation that LSR-specific methods are planned and reported in the relevant sections of the methods of the protocol.

LSRs build on a standard Cochrane Review

- Whether an author team is publishing a new review, or transitioning an existing review, there will need to be up-to-date 'baseline' review to build upon.

LSRs utilise existing publication platforms and processes

- Our LSR model makes use of the Updating Classification System (1), as a way to provide updates to readers, without always having to re-publish the Cochrane Review each time.

- However, if new evidence is incorporated to the review, the standard updating processes apply, and all sections of the review must be updated and republished.

Principles underpinning the Cochrane Living Systematic Review model

We applied the following principles 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, peer reviewers, editors, publishers)
- Maximise visibility of the latest findings for the reader
- Maximise efficiencies through technology and involving the crowd
- Streamline workflows and editorial processes
- Don't reinvent the wheel, but build on existing processes and platforms
- Focus on workable, not perfect, solutions
- Remain flexible to incorporate new developments in broader evidence ecosystem

The proposed Cochrane Living Systematic Review model is presented diagrammatically in Figure 2, followed by a narrative description in text and Table 3.

FIGURE 2. DIAGRAMMATIC REPRESENTATION OF PROPOSED COCHRANE LSR WORKFLOW, WITH PUBLICATION OUTPUTS
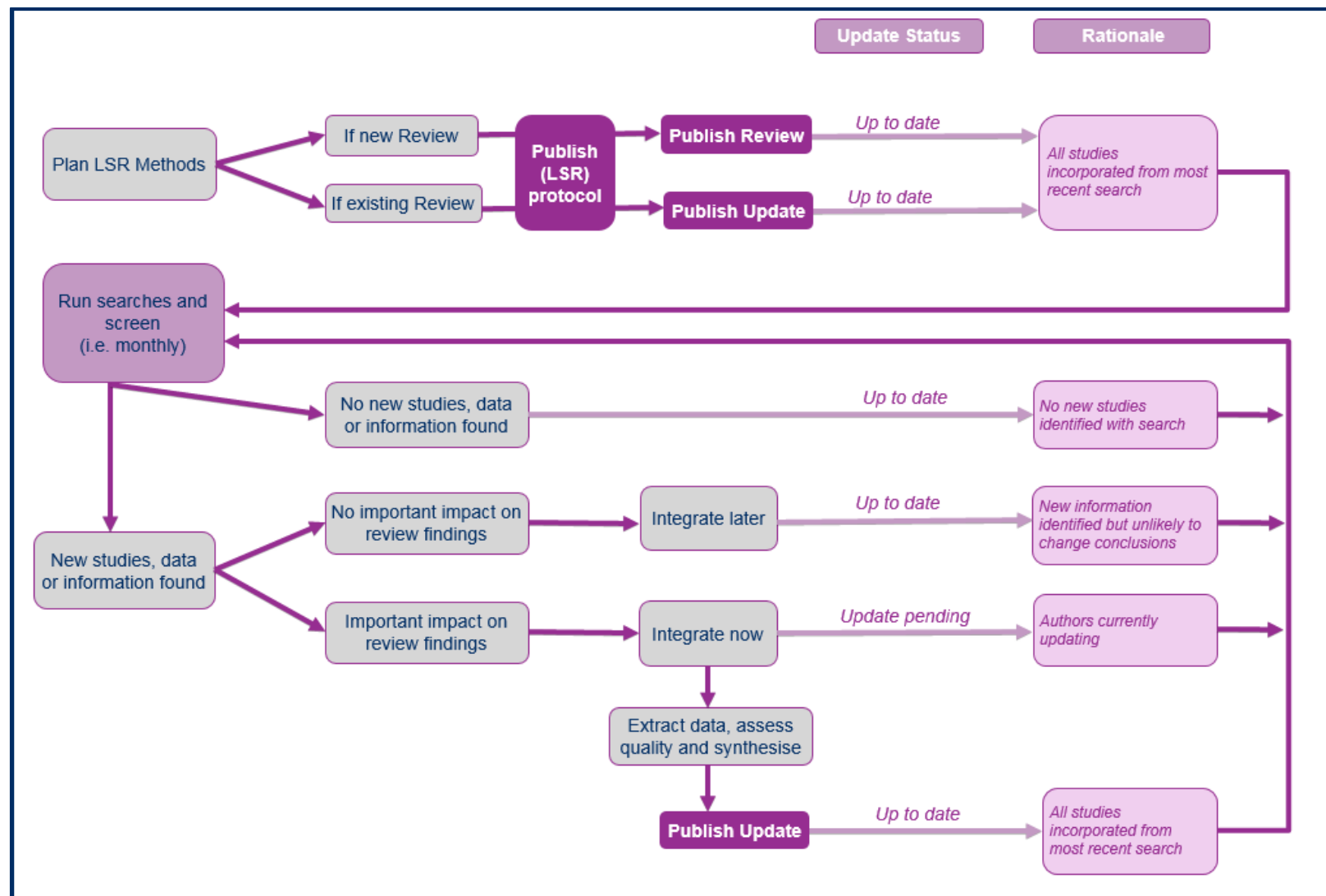
Protocol stage

Planning LSR methods

Living systematic reviews require that additional specific methodological decisions are made and reported prior to the review being conducted. All LSR-related methods should, and can be, incorporated into the standard headings of a Cochrane protocol, and Review.

A protocol for a Cochrane LSR will include all the usual information that is reported in a standard Cochrane protocol. There will also be additional information relating to search methods and frequency, and deciding when and how to integrate studies.

Guidance relating to these specific methodological considerations, along with suggested text is provided the Protocol template (See Appendix 2).

Publishing LSR methods

How to publish the planned LSR methods for a Cochrane Review may be different depending on whether the LSR is being undertaken as a new Review, or an existing LSR will be transitioned into an LSR.

For new reviews, it is straightforward to:

- Incorporate the planned LSR methods into the Protocol for the Review
- The protocol is then published according to standard Cochrane processes.

For existing reviews, the preferred option is currently to:

- Update the review, and publish it on the Cochrane Library, with the LSR protocol added to the appendices of the review.

NOTE: The preferred approach for publishing the LSR-relevant methods for existing Cochrane Reviews may change with the launch of the Enhanced Cochrane Library, due later in 2017

Review stage

How a Cochrane Living Systematic Review is produced and published at the review stage is explained in detail in the following section. To aid this description, a comparison table has been developed, outlining 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 updating status implications (see Table 3).

TABLE 3. COMPARISON OF AUTHOR TEAM AND EDITORIAL ACTIVITIES, PEER AND EDITORIAL REVIEW AND PUBLICATION PROCESS, BETWEEN COCHRANE LSR SCENARIOS

		Initial review	Once review becomes living			
		'Baseline' Cochrane Review	Scenario 1: No new evidence	Scenario 2: New evidence, no impact, integrate later	Scenario 3: New evidence, important impact, integration in process	Scenario 4: New evidence, important impact, integrate now
Production activities	**Authors** Alert ME	✗	✓	✓	✓	✓
	Edit RevMan file	✓	✓	✓	✓	✓
	Submit RevMan file	✓	✗	✗	✗	✓
	Managing Editor Enters LSR UCS	✓	✓	✓	✓	✓
	Other	Secures LSR reviewers		Reviews authors' decision		Applies peer review policy
	RevMan file (mode)	Authoring to Editorial, then Publish	Authoring	Authoring	Authoring	Authoring to Editorial, then Publish
Editorial and peer review	**Editorial review?**	✓	✗	✓	✗	✓
	Peer review?	✓	✗	? (if req'd for second opinion)	✗	✓ (in line with peer review policy)
Cochrane Library	**Cochrane Review publication**	New Review / Update	Unchanged	Unchanged	Unchanged	Update
	Update Status on Library	Up to date	Up to date	Up to date	Update pending	Up to date
	Update Rationale on Library	All studies incorporated from most recent search (item 7)	No new studies identified with search (item 6)	New information identified but unlikely to change conclusions (item 11)	Authors currently updating (item 13)	All studies incorporated from most recent search (item 7)

Abbreviations: LSR = Living Systematic Review, ME = Managing Editor, RevMan = Review Manager, UCS = Updating Classification System.

Establishing a 'baseline' Cochrane LSR

Irrespective of whether the LSR is commenced as a new Review or an Update, there needs to be an up-to-date Cochrane Review published on the Cochrane Library. This is effectively a 'baseline' review. Only at this point will the 'living' part of the LSR commence, for the reader (although the author team is likely to have already set up their searches and be screening the yield regularly, in anticipation for the review becoming living).

The Review should be conducted in accordance with Cochrane's Methodological Expectations of Cochane Interventions Reviews (MECIR) guidelines (5), and proceed to publication following standard Cochrane processes. All eligible studies should be fully integrated in the review, and the planned LSR methods should be outlined in the Methods section.

There are two key procedural differences between a 'baseline' Cochrane LSR and standard Cochrane Review for Managing Editors.

1. ### Selecting peer reviewers

   The Managing Editor would ideally seek the approval of the peer reviewers to be available for peer review of subsequent LSR updates. Note that the frequency of their involvement would vary depending on how frequently new studies are identified, whether they were to be immediately incorporated into the review, and whether any full updates of the Review required full/specialised/no peer review.

2. ### Using an amended Updating Classification System

   The Managing Editor would apply the Updating Classification that has been specifically tailored for LSRs. The Update Status and Update Rationale for a 'baseline' review (see Table 3) is drawn from existing options in the Updating Classification, but the Update Explanation is amended, as per below:

Status	Up to date
Rationale	All studies incorporated from most recent search (item 7)
Explanation	This is a Living Systematic Review. Searches are run and screened monthly. Last search date XX. Results of all new studies identified have been incorporated. The conclusions of this Cochrane Review are therefore considered up to date.

Preparation for transition to LSR

Once the 'baseline' Review is published, the review immediately becomes a Living Systematic Review on the Cochrane Library. In practice, this means that the searches are run and screened at their pre-determined frequency (i.e. monthly, although the author team is likely to have commenced this process some months earlier), and the outcome of this screening regularly communicated to the reader on the Cochrane Library.

There are two things that must happen at this point:

1. ### Review goes into authoring mode

   The Managing Editor should return the review into authoring mode in RevMan. This will allow the team to make any updates to the material over time (i.e. keep the PRISMA or characteristics of excluded studies updated) so that when the time comes to re-publish the review, they will have most of the new evidence already incorporated into the manuscript.

2. ### Search alerts commence (if not already)

   The author team is likely to have already set their search alerts when they ran the searches for the 'baseline' Review, but if not, search alerts are set up immediately. The searches should be run and screened at the frequency specified in the methods.

Once the review is living

Each time the searches are run and screened, there may or may not be new studies identified, and they may or may not warrant immediate inclusion in the review.

In the instances that no new studies are identified, or new studies are identified but they will not change the review conclusions in a meaningful way, this can be managed by the Updating Classification System.

There are four possible scenarios:

1. **No new evidence (studies, data, information) identified**

2. **New evidence, no important impact on review findings, integrate later**

3. **New evidence, important impact on review findings, integration in progress**

4. **New evidence, important impact on review findings, integrate now**

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 the publication and updating status implications. The detail below supplements the information in Table 3.

Scenario 1: No new evidence identified

In scenario 1, the team screens their monthly yield and find no new evidence (i.e. studies, data or information) to include in the review.

Production activities

The Author team emails the Managing Editor to advise that no new evidence has been found with the most recent search. The RevMan file remains in the authoring mode, allowing the author team to incorporate the results of this search (i.e. PRIMSA, or adding any excluded studies to the review).

The Managing Editor amends the Updating Classification in Archie (see Proposed LSR Update Classification for Scenario 1), which will appear on the Cochrane Library immediately.

Editorial and peer review

Editorial and peer review is not required (manuscript unchanged).

Cochrane Library publication

The published Cochrane Review remains unchanged, but the Updating Classification is amended, as per below.

Status	Up to date
Rationale	No new studies identified with search (item 6)
Explanation	This is a Living Systematic Review. Searches are run and screened monthly. Last search date XX. 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, no important impact on review findings, integrate later

In Scenario 2, new evidence is identified in the monthly search but the authors and the editorial team judges that it is likely to have no important impact on the review findings.

Production activities

The author team emails the Managing Editor to advise that new evidence (studies, data or information) has been found with most recent search, but was judged to have no important impact on review findings, for integration later. This decision should be justified. This judgement should be made in line with guidance in Updating Classification System: guide to applying to Cochrane Reviews (1), and would have been pre-specified in the Methods section of the Review. The review remains in authoring mode, and the authors may choose to incorporate the results of most recent search (i.e. PRIMSA, or adding newly included evidence, revising text) to the RevMan file.

The Managing Editor reviews this decision with the editorial team, and may decide to seek the opinion of one of the peer reviewers (see Editorial review). Once confirmed, they amend the Updating Classification in Archie (see Proposed LSR Update Classification for scenario 2), which will appear on the Cochrane Library immediately

Editorial and peer review

The author teams' decision requires editorial review and approval. Rather than full peer review (there is no new manuscript), an opinion may be sought from one of the peer reviewers.

Cochrane Library publication

The published Cochrane Review remains unchanged, but the Updating Classification is amended, as per below.

Status	Up to date
Rationale	New information identified but unlikely to change conclusions (item 11)
Explanation	This is a Living Systematic Review. Searches are run and screened monthly. Last search date XX. A new stud(ies) has(ve) been identified in a recent search [hyperlink to DoI] but the new information is unlikely to change the review findings (as assessed by the authors and editorial team). The conclusions of this Cochrane Review are therefore considered up to date.

SCENARIO 3: New evidence identified, important impact on review findings, integration in progress

This scenario applies where there is likely to be a time lag of a few weeks while new studies are being integrated, and the review undergoes editorial and possibly peer review, prior to publication. As such, Scenario 3 is offered as an <u>interim scenario</u>, whereby the reader can be alerted to the fact that the review is no longer up to date, but the update is in progress.

Production activities

The author team emails the Managing Editor to advise that new evidence (studies, data or information) has been found with most recent search that was judged to have an important impact on review findings. The authors advise the Managing Editor that a new update has commenced. The review remains in authoring mode, and the authors start incorporating the new evidence to the RevMan file.

The Managing Editor amends the Updating Classification in Archie (see Proposed LSR Update Classification for scenario 3), which will appear on the Cochrane Library immediately

Editorial and peer review

Editorial and peer review is not required until submission of the manuscript (see Scenario 4).

Cochrane Library publication

The published Cochrane Review remains unchanged, but the Updating Classification is amended, as per below.

Status	Update pending
Rationale	Authors currently updating (item 13)
Explanation	This is a Living Systematic Review. Searches are run and screened monthly. Last search date XX. In a recent search, a new stud(ies) was(were) found that is (are) currently being included in the review [hyperlink to DoI]. The update is due to be published [month/year]

SCENARIO 4: New studies identified, likely to change conclusions, integrate now

Scenario 4 is essentially a new review update, publishing according to standard Cochrane procedures. Scenario 4 may follow scenario 3 (i.e. the author team now has capacity to include the study), or it may arise following a monthly search, and the team decides to immediately incorporate the new evidence.

Production activities

Author team advises the Managing Editor and commences continues working on full update. They submit to the editorial base for publication, as per standard processes.

Once submitted, the Manager Editor follows standard processes to proceed to publication. Once published, they amend the Updating Classification (see Proposed LSR Update Classification for scenario 3), which will appear on the Cochrane Library immediately.

Editorial and peer review

The updated review should undergo standard editorial review prior to publication. The need for full versus selective peer review should be made in accordance with the Cochrane peer review policy (currently out for consultation (6)).

Cochrane Library publication

New publication on the Cochrane Library. The fact that it's a new version of the review will be captured in the What's New box, as per standard process with an updated review. The Updating Classification can be amended as per below.

Status	Up to date
Rationale	All studies incorporated from most recent search (item 7)
Explanation	This is a Living Systematic Review. Searches are run and screened monthly. Last search date XX. Results of all new studies identified have been incorporated. The conclusions of this Cochrane Review are therefore considered up to date.

Publishing Living Systematic Reviews

Publication of living systematic reviews poses several challenges in publishing systems designed for standalone or relatively infrequently updated systematic reviews.

In considering how best to publish LSRs within the existing Cochrane Library infrastructure we have weighed up a number of different factors including the implications for DoI/citation, impact on author and editorial teams (both workload and other), visibility in systems such as CrossMark and PubMed, and the experience for the LSR user; as well as the available functionality of the Library in its current form (see Table 4).

The approach we have outlined means that the most up-to-date information on the status, progress and content of the review is rapidly available on The Cochrane Library, (using the Updating Classification mechanism) and changes to the review content are available in other systems when the LSR is formally updated to reflect new evidence.

Future versions of the Cochrane Library may support richer, more dynamic publication of LSRs, for example enabling access to regularly updated review components such as Summary of Findings tables (see Table 4).

TABLE 4. OVERVIEW OF CURRENT AND FUTURE PUBLISHING OPTIONS TO DISPLAY A LIVING SYSTEMATIC REVIEW WITH CORRESPONDING IMPLICATIONS

	CURRENT OPTIONS			FUTURE OPTIONS	
	Proposed model	Alternative model 1	Alternative model 2	Enhanced Cochrane Library (from 2017)	Ideal model (beyond 2017)
Description	Utilise Updating Classification System	Fully revised and updated Review manuscript with every search	Short, standalone summaries of newly included studies (Targeted Update- model, or web-based?)	Future LSR publishing options will be informed by the functionality of the enhanced Cochrane Library post launch in 2017.	A number of models are possible, including, for example, allowing component parts of reviews to be made available with shorter commentaries that add value for Cochrane and the reader / user while reducing time and resources to produce
New DoI / citation?	✗	✓	✗ (Not a formal publication)		
Author & editorial impact	Minimal	Significant ++	Moderate (Editorial and peer review implications unclear. Authors need agreed format)		
Shown via CrossMark?	? or ✓ (Probably)	✓	✗ (External to published article)		
Visibility in PubMed?	✗ But could be flagged in abstract, i.e. 'This is a Living Systematic Review. Check the Cochrane Library for updates'.	✓ New, linked PubMed entry	✗ Could be flagged in abstract as per 'Proposed' model		
Visibility on Cochrane Library?	✓ Update Status prominently displayed	✓ Latest update replaces previous version	? Unclear how / where new summary material would be linked		
Reader Experience	-Manuscript not always up to date -But key information (search date, update status, DOI of yet to be included studies) clearly flagged	-New readers will always see complete, up-to-date article -For returning readers, latest changes may not be clear	-Summary and any commentary presentation would be key for reader to understand its link. -Difficult to cite correctly		

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" (2) (p.287), the time, effort, and skill required have been insurmountable barriers to achieving that vision. However, recent innovations such as those in table 2 now mean that many of those barriers can be substantially reduced, and potentially overcome.

Development in machine learning and automation, along with citizen science initiatives, can massively reduce the burden of effort place on authors to screen search results. Author support tools and online task sharing tools provide opportunities to support and manage diverse, collaborative author teams. New approaches to quality assurance and publication enable rapid publication of high-quality reviews. Taken separately, each of these innovations presents a valuable opportunity to produce better reviews quicker. Taken together they may enable an entirely new paradigm of review production.

TABLE 2. LSR ENABLERS (ADAPTED FROM ELLIOTT ET AL (3))

Category	Item	Description
Production	*Workflow and collaboration tools*	Tools and platforms for SR authoring (e.g. Covidence, EPPI-Reviewer)
	Semi-automation	Machine assisted SR production processes (e.g. Project Transform Evidence Pipeline, Robot Reviewer, RevMan HAL)
	Data repositories and linked data	Repositories of structured SR data (e.g. Cochrane Linked Data Project)
	Participation and the crowd	Large and diverse author groups, citizen and crowd participation, nanopublication (e.g. TaskExchange, Cochrane Crowd)
Publication	*Innovations in peer and editorial review*	Adaptations to conventional peer and editorial review (e.g. new Cochrane peer review policy)
	New forms of scholarly communication	Attribution, citation and listing in electronic databases (e.g. threaded publications, linked DOIs)

Key considerations for authors and editors before commencing a Living Systematic Review

All systematic reviews require substantial time and resource inputs from authors and editorial teams. However, LSRs require a sustained commitment, for the duration of time that the review remains living.

As such, additional considerations include whether:

- The author team have capacity and resources to sustain an ongoing SR commitment (acknowledging that the author team may evolve over time)
- The editorial base is able to support a Cochrane Review as an LSR

Some key questions for authors and editors

- Who takes responsibility for project management, i.e. managing the search alerts, distributing workload etc.?

- Would you be prepared to handover leadership of the LSR if you and your team were no longer able to sustain it, and another team was able and willing?

- Do you have two or more authors who can screen on an ongoing 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 over time?

- What is your plan to manage authorship implications and expectations?
    - It is expected that the author team will evolve over time
    - Standard authorship considerations apply (i.e. Cochrane Handbook, section 4.2.2)
    - Over time, new authors can be added to the list, and previous contributors can be moved to the Acknowledgements

# A vision for the future of Living Systematic Reviews

Vision for the future of Living Systematic Reviews

The approach to LSRs outlined in this document is a first step towards a richer, more innovative vision of LSRs as a key component of a new, dynamic, evidence ecosystem (Figure 1). In this vision, LSRs substantially enhance the efficiency and opportunities for translation of research results into improved health care.

In the current health knowledge ecosystem (inner circle) inefficiencies hamper the flow of knowledge from health practice through primary research, systematic review and guidelines, and finally back to impacts on health practice.

The emerging health evidence ecosystem (outer circle) will be characterized by a continuous flow of data from efficient, near real-time systems, including the growing contribution of 'learning health care systems', which together with individual participant data and traditional published research will provide an increasingly large, rich and complex set of data.

Semi-automation and crowd sourcing techniques for processing and synthesising these data, together with structured and reusable 'linked' data formats, will enable LSRs to incorporate increasingly diverse and complex data and link to living guidelines, standards, policies, and decision support systems, closing a "living" health knowledge loop (3).
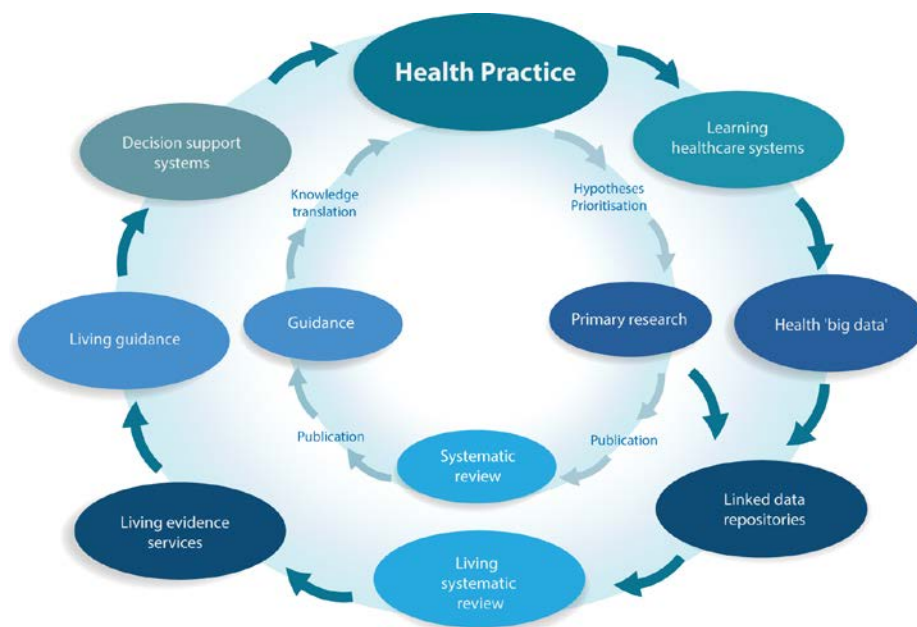
FIGURE 1. CURRENT AND EMERGING HEALTH KNOWLEDGE ECOSYSTEMS (FROM ELLIOTT ET AL, 2014).

Cochrane can lead the field in Living Systematic Reviews

Systematic review authors and publishers within and beyond Cochrane are starting to explore different approaches to producing, maintaining and disseminating LSRs. Cochrane is well-placed to lead the developments in this area, for the following reasons:

1. We already publish updates

Unlike almost all other producers of systematic reviews, Cochrane has an existing culture and practice of undertaking and publishing systematic review updates, so moving to a living publishing model is conceptually, and practically more achievable. With The Cochrane Library, we already have a publication platform, and associated editorial processes, that can manage multiple, updated versions of reviews and flag 'What's New' for the reader. This gives Cochrane a very significant advantage over many journal publishers, who do not have the systems or established workflows to handle updated manuscripts and information.

2. We have the methodological expertise

Cochrane's greatest asset has always been its international community of engaged and expert researchers and contributors. Cochrane contributors remain at the forefront of methodological research into systematic reviews and LSRs are no exception. Coordinated by Cochrane, many of the leading researchers involved in developing LSRs and LSR methods internationally have come together as part of the LSR Network, with the explicit goal of developing and testing candidate approaches for LSR pilots within Cochrane.

3. We are investing in the 'enablers'

Cochrane is developing many of the key enablers of LSRs such as text mining, machine learning, citizen science platforms, author support tools, and linked data as part of Project Transform, the Linked Data Project and Cochrane's Author Support Tools. These innovations provide an opportunity to continuously assess and curate the evidence base for Cochrane LSRs in a systematic, efficient and collaborative way.

Opportunities related to Living Systematic Reviews

Living systematic reviews present several potential related benefits to Cochrane. These include increasing the value of Cochrane products for users; increasing the uptake of the results of Cochrane reviews; and increasing the opportunities for contributors to collaborate with Cochrane.

Increasing the 'value' of Cochrane's products to our users

Living systematic reviews provide an opportunity to increase the value of a Cochrane review to users by making available more useful information on the current status, progress and content of the review and its components. For example, LSRs ensure that the most recent search date is always available, and provide links to new studies which have been identified but not yet incorporated. Future iterations might make other review components available to users as they are created and reviewed, before the full review update is made available.

The LSR 'approach' is more about maintaining an up to date dataset, and giving the reader/user as much useful information as possible, at all times, rather than focusing on a single 'perfect', traditional publishing solution.

Increasing the dissemination and uptake of the results of Cochrane reviews

As the definition of LSRs provided earlier indicates, LSRs should be tightly linked into a living dissemination process; a proactive and ongoing process of translating the updated results of the review into tools that can support evidence-based decision-making in health practice and policy.

Many of the current examples of LSRs are being driven by links to guideline development processes, and future updates of these reviews will then be supported by the desire to make these guidelines (or their recommendations) 'living' or continuously updated in light of new evidence. Living guidelines are likely to be both the trigger for commencing a Living Systematic Review, and the output into which an LSR directly feeds.

Increased opportunities for potential Cochrane contributors

Living systematic reviews provide an opportunity to increase collaboration in the conduct of reviews. Innovative LSR approaches such as that promoted by Badgett et al (7) (e.g. https://openmetaanalysis.github.io/) provide platforms for open, collaborative, Wiki-like production and dissemination of LSRs. Other teams are using online technologies to enable collaboration among members of larger, but still-closed, review teams (8, 9).

Cochrane may find that tools such TaskExchange, Cochrane Crowd, Covidence and EPPIReviewer enable new methods of bringing together author teams and coordinating production of living systematic reviews. These new approaches may enable a wider, more diverse collaborative community within Cochrane, and provide new entry points for new Cochrane contributors.

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Appendix 1. List of contributors

Many members of the Living Systematic Review Network contributed to the conceptualisation of LSRs that informed this document, or provided verbal or written feedback on document drafts.

Living Systematic Review Network members as at 21 April 2017 include:

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Appendix 2. Cochrane LSR protocol template

Methods considerations specific to LSRs	LSR protocol suggested text and/or examples
Background	
Description of the condition; Description of the intervention; How the intervention might work	
No changes proposed	N/A
Why it is important to do this review	
It should be clear to the reader why a Living Systematic Review approach is appropriate for your Cochrane Review. LSRs build on recent guidance (4) about when a systematic review update is appropriate. Broadly speaking, an LSR may be appropriate when all three of the following criteria are met: ● 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 the existing evidence ● There is (likely to be) emerging evidence that will impact on the conclusions (i.e. in trial registers).	<u>Suggested text</u> No suggested text is provided, given this will vary from review to review. <u>Example 1</u> "We have previously shown that, when considered collectively, 29 systematic reviews of second-line treatments in advanced NSCLC published from 2001 to 2015 did not encompass the whole available randomised evidence, with more than 40% of treatments, treatment comparisons and trials missing. There are no broad MAs encompassing all available treatments, and which treatments work the best remains unclear (…) Another potential concern is that when MAs exist, only very few are updated (…) To account for the need to cover all available evidence, address the lack of some treatment comparisons and to update constantly, we have proposed a new paradigm called 'live cumulative NMA'". (8), p.2
Objectives	

Methods considerations specific to LSRs	LSR protocol suggested text and/or examples
It is appropriate, and likely to be helpful for the reader, to make the fact that this review will be updated using an LSR approach explicit in the objectives. Rather than altering the main objective(s), this can be added as a second, or subsequent, objective.	<u>Suggested text</u> "A secondary objective is to maintain the currency of the evidence, using a Living Systematic Review approach."
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
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 (typically <u>monthly</u>). Search frequency 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.	<u>Suggested text</u> **Living Systematic Review considerations** [NEW Level 3 heading at end of this section] "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."

Methods considerations specific to LSRs	LSR protocol suggested text and/or examples
Search strategies may 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 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 newer Cochrane developments like the Evidence Pipeline and Cochrane Crowd).	Example 1 See Fig 2 in Crequit (8) which outlines a detailed adaptive search strategy, with search frequency for bibliographic databases, clinical trial registries and conference abstracts (every 4 months) and regulatory agencies, industry trial registries and health technology assessment agencies (yearly).
Searching other resources	
Searching additional sources may need to be undertaken at the same frequency as database or electronic sources. For some 'Other sources' such as websites or annual conference proceedings, less frequent searching may be appropriate (but no less frequently than yearly). This should be clearly described in the protocol.	**Living Systematic Review considerations** [NEW Level 3 heading at end of this section] "For the following other resources [insert any websites or other sources, etc listed in 'Searching other resources'] we will search these resources every month [or insert appropriate frequency], via auto-alerts, or manually. We will note when key conferences are held and search their conference proceedings when published. We will contact corresponding authors of ongoing studies as they are identified and ask them to advise when results are available, or share early or unpublished data. The corresponding authors of any newly included studies will also be contacted for advice as to other relevant studies. To conduct citation tracking of included studies on an ongoing basis, we will set up citation alerts in Web of Science Core Collection [or preferred database source]. We will manually search the reference list of any newly included studies."

Methods considerations specific to LSRs	LSR protocol suggested text and/or examples
	Example 1 See Fig 2 in Crequit (8) which outlines an adaptive search strategy, with search frequency for bibliographic databases, clinical trial registries and conference abstracts (every 4 months) and regulatory agencies, industry trial registries and health technology assessment agencies (yearly).
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. LSRs will often use some of Cochrane's newer systematic review enablers, such as the RCT Classifier (via CRS-Web) and Cochrane Crowd. How this will be used in your LSR should be made explicit.	Suggested text **Living Systematic Review considerations** [NEW Level 3 heading at end of this section] "We will screen any new citations retrieved by the monthly searches immediately." [Note, the following text relates to the first LSR pilot. Other reviews may use different approaches, and some may not use any technological enablers.] "Before screening the search yield, we will apply the machine learning classifier (RCT model) available in the Cochrane Register of Studies (CRS-Web). This provides a probability (from 0 to 100) of each citation being a true RCT. For citations that are assigned a probability score of less than 10, the RCT classifier currently has a specificity/recall of 99.987% (Thomas, personal communication). Citations assigned a score from 10 to 100 will be screened

Methods considerations specific to LSRs	LSR protocol suggested text and/or examples
	independently by two authors. Citations that score 9 or less will be screened by Cochrane Crowd (crowd.cochrane.org). Any citations that are deemed to be potential RCTs by Cochrane Crowd will be returned to the authors for screening."
Data extraction and management, Assessment of risk of bias of included studies	
No changes proposed	N/A
Measures of treatment effect, Dealing with missing data, Unit of analysis issues	
No changes proposed	N/A
Assessment of heterogeneity, Assessment of reporting biases	
No changes proposed	N/A
Data synthesis	
Deciding when to incorporate new evidence During the life of a Living Systematic Review, it is expected that review teams will identify not just 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, or a now completed trial may remain unpublished. Given that Living Systematic Reviews are only likely to be undertaken on	Suggested text **Living Systematic Review considerations** [NEW Level 3 heading at end of this section] Whenever new evidence (meaning studies, data or 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. OR

Methods considerations specific to LSRs	LSR protocol suggested text and/or examples
topics for which new evidence is likely to have an important impact on the review, the default position should be that new studies and any important new data or information should be incorporated into the review. However, there may be instances where the new studies, data or information does 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. They can flag the existence of this new information to the reader using the update status classification. 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(4) (See Step 3: assess the effect of updating the review).	Whenever new evidence (meaning studies, data or 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 outcomes • The credibility (e.g. GRADE rating) of one or more outcomes • New settings, populations, interventions, comparisons or outcomes studied • Other [author teams to determine] [Note, for refinement in first LSR pilots]
<u>Any adjustments for frequent meta-analyses</u> NOTE: Further being sought from statisticians within Cochrane and LSR Network for recommended approaches to managing statistical implications of a priori, prospective meta-analysis and frequent updates.	<u>Suggested text</u> [Proposed text to be added when developed for first LSR pilots]
Subgroup analysis and investigation of heterogeneity, Sensitivity analysis, Summary of Findings Table	
No changes proposed	N/A
Methods for future updates	<u>Suggested text</u> **Methods for future updates**

Methods considerations specific to LSRs	LSR protocol suggested text and/or examples
[This is an optional heading in RevMan, which can be activated for LSRs] <u>When review methods will be reviewed</u> In an LSR approach, authors won't necessarily have the same trigger to review the methods for any necessary revisions, in the same way that they currently do with separate review updates. Authors should pre-specify when they will review the methods. <u>The conditions under which the review will no longer be maintained as an LSR</u> It is anticipated that reviews may cease to need to be living over time, as the review findings become stable, 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 a LSR, acknowledging it is difficult to predict all future possible scenarios.	[ACTIVATE Level 3 heading in this section of the protocol] 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 or outcomes, or new review methods available). <u>Suggested text</u> No proposed text developed on 'The conditions under which the review will no longer be maintained as an LSR' giving these may be different for different reviews. <u>Example 1</u> [Example to be generated in first LSR pilots]