Dynamic System Evaluation Production Method and Process Postprint

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Abstract

Living systematic review is a continuously updated systematic review methodology that aims to incorporate new evidence in a timely manner, ensuring that healthcare professionals and policymakers can access the latest information to make optimal decisions. Compared with traditional systematic reviews, living systematic reviews regularly search for, screen, and analyze new evidence, thereby ensuring the timeliness and accuracy of information to better meet the demands of rapidly evolving clinical practice. This article compares living systematic reviews with traditional systematic reviews and rapid reviews, aiming to introduce their applicable conditions, development methods, and procedures; explore the challenges and opportunities encountered during implementation; and illustrate the key steps in their development process and dynamic updating through examples, thereby providing reference and guidance for scholars developing living systematic reviews.

Full Text

Living Systematic Reviews: Methods and Processes for Development

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Abstract

Living systematic reviews (LSRs) represent an evolving methodology for systematic review that is continuously updated to incorporate new evidence in a timely manner, ensuring that healthcare professionals and policymakers have access to the most current information for optimal decision-making. Compared to traditional systematic reviews, LSRs ensure the timeliness and accuracy of information by conducting regular searches, screenings, and analyses of new evidence, thereby better meeting the needs of rapidly changing clinical practice. This article introduces the applicability, production methods, and processes of LSRs by comparing them with traditional systematic reviews and rapid reviews, discusses the challenges and opportunities faced during implementation, and illustrates the production process and key aspects of living updating with examples, aiming to provide scholars with references and insights for conducting LSRs.

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Evidence-based medicine integrates clinical practice with physicians' personal experience, patient preferences, and research evidence from systematic evaluations and syntheses, with its core principle being that medical decisions should be based on the best available current evidence [1]. As the highest level of evidence in the evidence pyramid [2], systematic reviews face challenges such as long evidence generation and update cycles during application, which compromise their accuracy and timeliness in meeting clinical practice needs [3]. Consequently, Elliott et al. [4] proposed living systematic reviews (LSRs) in 2014—systematic reviews that are continuously updated by timely incorporating new research evidence as it emerges. The Cochrane Collaboration defines LSRs as systematic reviews that conduct regular searches and screening for new research evidence related to the question of interest and carefully consider whether immediate updates are needed when new evidence becomes available [5]. LSRs are distinct from rapid reviews (RR), which accelerate the systematic review process by simplifying or omitting certain methodological steps to efficiently

utilize resources and produce evidence more quickly [6]. The differences among SRs, LSRs, and RRs are presented in Table 1 . This article introduces LSRs by discussing their applicability, production processes, challenges, and advantages, aiming to provide scholars with references for developing LSRs.

1 Applicability of Living Systematic Reviews

LSRs are suitable for the following situations [3, 11]: (1) The key question addressed by the systematic review is a priority for decision-making. During the production and publication process, the PICO (population, interventions, controls, and outcomes) question addressed by the systematic review is sufficiently important for decision-making to warrant continuous resource investment. Over time, the PICO scope of the LSR may be appropriately expanded. (2) The certainty of existing evidence is low or very low. Current evidence cannot provide definitive conclusions, and new research may alter the systematic review' s findings. (3) New research is likely to emerge. The research field covered by the systematic review is developing relatively rapidly with continuous emergence of new studies [11, 13]. However, LSRs are not permanent; when the key question is no longer a decision-making priority, conclusions no longer change with new evidence, required resources become unavailable, or new evidence is no longer likely to emerge, the systematic review exits the living update mode [14].

2 Production Process for Living Systematic Reviews

As a systematic review methodology emphasizing timely evidence updates, the LSR production process is similar to traditional systematic reviews but with some differences. This article introduces its production methods and processes across four phases: preparation, production, updating, and writing/publication/dissemination.

2.1 Preparation Phase

Before initiating an LSR, adequate preparation is required, including topic selection, team formation, and protocol development and registration.

(1) Topic Selection and Research Question Definition. The optimal topic emerges at the intersection of clinical needs and the intrinsic development logic of clinical interventions. Whether the topic is appropriate, clear, and well-defined determines the significance, feasibility, and overall protocol design of the LSR [15]. LSR topics can be selected using traditional systematic review methods (i.e., developing a de novo best-topic systematic review) or by updating existing systematic reviews. Based on the selected topic, structured question models such as PICO are used to define the LSR research question. Different fields employ different question formulation approaches: for therapeutic areas, questions can be structured as PICO; for qualitative research, as SPIDER (samples, phenomenon of interest, design, evaluation, research); and for incidence and prevalence questions, as CoPop (condition, context, population) [16].

(2) Team Formation. LSR production team composition typically mirrors traditional systematic reviews, including systematic review methodologists, search specialists (e.g., librarians), statisticians, and clinicians [15]. However, compared to traditional systematic reviews, LSRs require continuous performance of searching, screening, appraisal, and analysis tasks, necessitating stronger team organization and management with timely adjustment of member tasks and schedules based on production progress. Additionally, online collaboration models such as "crowd sourcing" or "task-sharing platforms" leverage network communities to aggregate human resources, dividing systematic review update tasks among more collaborators for synchronous, rapid completion, thereby improving LSR production efficiency [3, 17-18].

(3) Protocol Development. LSR protocols build upon traditional systematic review protocols by explicitly stating the rationale for living updates, describing search frequencies for each database and screening frequencies for results, clarifying principles and timing for integrating new evidence into existing systematic reviews, specifying frequencies for reviewing the appropriateness of search methods, strategies, and statistical analysis methods, and defining criteria for exiting the living update mode (Table 2). LSR protocols require continuous revision over time, with methodological changes during production documented in the protocol.

(4) Registration. Before commencing research, LSRs can be registered on the COCHRANE registration platform (https://www.cochrane.org/), the International Prospective Register of Systematic Reviews PROSPERO (https://www.crd.york.ac.uk/PROSPERO/), or the International Platform of Registered Systematic Review and Meta-analysis Protocols INPLASY (https://inplasy.com/) to protect research originality and foresight, avoid duplication, and reduce reporting bias. Cochrane provides writing guidance with longer review cycles, covering systematic review titles, protocols, and full texts. PROSPERO has shorter review cycles, reviewing only titles and protocols without providing writing guidance. INPLASY has short review cycles but charges fees for registration and updates [15].

2.2 Production Phase

The production of the first LSR version follows the same process as traditional systematic reviews, including developing search strategies and inclusion/exclusion criteria, literature searching and screening, bias risk assessment and data extraction, data analysis, and certainty of evidence evaluation. During this process, relevant technologies can be employed to accelerate systematic review production (Table 3).

A critical consideration during dynamic updates is that when applying LSR results to decision support (e.g., making clinical decisions, developing clinical practice guidelines), assessment of evidence certainty involves issues of imprecision, requiring consideration of Type I error (false positives, typically caused by

repeated meta-analyses) and Type II error (false negatives, typically caused by insufficient sample size) [3, 20]. To reduce these risks, Simmonds et al. [20] recommend using trial sequential analysis (TSA), sequential meta-analysis (SMA), Shuster' s method, and the law of the iterated logarithm (LIL). These methods are also applicable to traditional systematic review updates.

Meta-analyses typically focus on direct comparisons between two interventions with relatively narrow clinical question scopes. Applying living update methods to network meta-analysis can overcome this limitation [21-22]. To encompass all evidence for all interventions (including both existing interventions in the network and new interventions), more comprehensive search strategies must be developed to incorporate subject headings and keywords related to new interventions [21-22]. Additionally, compared to standard meta-analysis methods, network meta-analysis also follows the alpha-splitting threshold principle under consistency assumptions. However, network meta-analysis involves high computational complexity. After each update, consistency assumptions must be re-evaluated. When few studies are included in the initial network meta-analysis, re-evaluating consistency assumptions can be challenging [3, 20].

2.3 Update Phase

Living systematic review updates primarily include three components: regular searching, new evidence assessment, and update implementation (Figure 1 [Figure 1: see original paper]) [3, 11, 23-24]. Regular searching aims to fully utilize database alert functions; for databases without this function, manual regular searching is required. Different databases can employ different search frequencies based on their update patterns. For example, major databases can be searched monthly, while secondary databases quarterly. Search results fall into two categories: new evidence generated or no new evidence generated [11, 23].

When no new evidence is generated, the LSR working group must inform users of the last search date and results. When new evidence emerges but is unclear or unlikely to substantially impact existing conclusions, it is recommended to delay integration into current results while informing users of the last search date, details of new evidence, and reasons for delayed inclusion. When new evidence would change systematic review results, it must be promptly incorporated, with users informed of the last search date, details of new evidence, and rationale for inclusion [11, 23]. Once inclusion of new evidence is determined, the subsequent update process initiates, including bias risk assessment, data extraction and synthesis, and results updating and interpretation. Status and information during the update process should be disclosed to users, with updated results published promptly. LSRs cease dynamic updating when they no longer meet living update requirements [11, 23].

2.4 Writing, Publication, and Dissemination Phase

LSR reporting can be either partial or full. Full reporting covers all sections of a systematic review including introduction, methods, results, and discussion. Partial reporting focuses on changes in the new version and information omitted from the previous version. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement for LSRs, PRISMA-LSR [25], is currently under development. Researchers writing LSR articles can refer to the PRISMA [26] and PRISMA-NMA [27] statements, presenting all information to readers as comprehensively as possible. In addition to information presented in these statements, researchers should explicitly describe [28]:

(1) **Rationale for adopting LSR:** The workload of systematic review production, peer review process, and manuscript publication all influence the use of "living" methods. Therefore, researchers must explicitly state that the current systematic review simultaneously meets all three applicability conditions for living update methods [28].

(2) **Methods for producing LSR:** Including dynamic literature search/screening frequency, data analysis methods, methods for publishing updated versions, and triggers for exiting living updates [28].

(3) **Changes in the new version of the systematic review:** Including five aspects: basic characteristics of the living review (additions and removals of authors, author contributions, conflict of interest declarations, and funding), methods (triggers for living updates, literature searching, inclusion criteria, literature screening, data extraction, bias risk assessment, data analysis, and certainty of evidence assessment), results (PRISMA flowchart, lists of included and excluded studies, effect sizes with 95% confidence intervals, bias risk and certainty of evidence assessment results, and conclusions), discussion (differences from previous versions or other studies on the same topic, recommendations for future research and practice), and peer review (whether each version is peer-reviewed, by whom, and whether full-text review is conducted) [28].

(4) **Update status of LSR:** Whether the LSR is still being updated; if so, whether new evidence has been incorporated and whether it has been integrated into the latest version [28].

Both the LSR protocol and the first version of the systematic review require editorial review and peer review before publication. Each update requires publication of relevant information or results, but the review process depends on the assessment of new evidence. If no new evidence is found, review may be omitted. If new evidence is delayed for inclusion, editorial or peer review may be selected based on actual circumstances. If new evidence is incorporated, editorial review and peer review are explicitly required [3, 11].

LSR publication and dissemination formats must accommodate frequent up-

dates. For publication platforms, options include open-access publishing platforms (e.g., F1000 Research) or CrossRef academic resource linking. Additionally, LSR publication requires appropriate author attribution mechanisms, with all authors required to comply with International Committee of Medical Journal Editors (ICMJE) standards. As personnel change over time, author lists and acknowledgments need to serve their respective functions [3, 11]. Furthermore, appropriate update publication frequency must be maintained. Overly frequent updates may reduce citation rates of individual papers, while overly slow updates may affect authors' academic output [3, 11].

In summary, the following publication models are recommended: (1) Publish the systematic review as a conventional paper while releasing regular update information on a dedicated independent website; (2) Publish both the systematic review and regular update information as conventional papers, but without independent DOIs for updates, preventing them from being cited as independent data sources; (3) Package the systematic review and regular updates in a more standardized format (e.g., F1000 Research platform) for publication [3, 11, 19]. Table 4 presents recommended publication and dissemination strategies for different evidence update statuses [19].

3 Challenges and Opportunities

Despite a decade of development, LSRs remain in their early stages, presenting several challenges during production, updating, and reporting.

3.1 Challenges in Production and Updating

(1) **Literature acquisition and screening.** LSRs require timely acquisition and screening of newly published studies for inclusion in the systematic review. As research volume increases, so does the workload of living updates, necessitating efficient methods and tools to quickly and accurately identify eligible literature while ensuring complete inclusion of new evidence.

(2) **Quality assessment and data extraction.** Systematic review teams must continuously extract key outcome data from newly included studies, assess study bias risk, and evaluate outcome certainty of evidence. Accurate assessment and data extraction of new evidence are critical steps ensuring result reliability and validity, requiring avoidance of bias from different members' subjectivity. For missing data, teams must employ appropriate methods for handling and sensitivity analysis.

(3) **Methodological development.** LSR implementation requires continuous attention to and adaptation of new methodological developments and guidance. Review teams must keep pace with methodological advances to ensure optimal research analysis methods are employed to avoid potential errors and bias [29].

(4) **Team stability and efficient collaboration.** LSRs require relatively

stable production teams to manage and maintain living updates, involving collaboration among multiple domain experts and stakeholders. Effective organization and coordination are needed to ensure timely information transfer and sharing. Team member engagement and collaboration capabilities are crucial for timely updates, requiring effective communication mechanisms for problem-solving and consensus-building.

(5) **Managing and maintaining update frequency.** LSRs require frequent result updates, necessitating pre-established feasible update plans and ensuring continuous maintenance. Teams must manage human, material, and financial resources to ensure process efficiency and quality. Therefore, teams must balance update frequency with resource constraints to ensure timeliness and quality.

(6) **Conflict of interest and author contribution management.** Due to demands for team member quantity and expertise, situations may arise where some authors join or leave core work mid-update or only participate in non-core tasks. Continuous management of team member conflicts of interest and reasonable assessment of individual contributions are required.

3.2 Challenges in Reporting

(1) **Update and maintenance frequency.** LSRs require regular, frequent result updates, meaning production teams must timely report results to stakeholders for application. Ensuring report accuracy and timeliness is challenging, requiring efficient coordination and management [28].

(2) **Result interpretation and presentation.** LSR reports must accurately present new evidence results, compare and interpret them with previous results, and clearly communicate the impact and changes new evidence brings to existing knowledge. Teams must appropriately interpret results to help users understand and apply findings.

(3) **Update reporting methods.** LSR update results must be timely disseminated to stakeholders, presenting a major challenge in conveying new versions while maintaining transparency [28].

Simultaneously, LSR development faces opportunities: (1) Since the COVID-19 pandemic, LSR methods have been widely applied by researchers, with methodological frameworks maturing to provide support for LSR production across different topics and evidence foundations for dynamic guideline development. (2) Literature searching, screening, and data extraction platforms based on artificial intelligence and machine learning (e.g., Covidence, Rayyan) not only accelerate systematic review production and greatly improve efficiency but also enhance accuracy at each production step. (3) LSRs can utilize collaboration platforms and crowdsourcing resources to engage broad stakeholders including researchers, decision-makers, and end-users, improving quality and relevance while increasing transparency and applicability. (4) With network technology

development, interactive dissemination platforms can be used to disseminate updated LSRs in user-friendly, accessible formats.

5 Case Example

This article uses the study "Systemic Immunomodulatory Treatments for Patients with Atopic Dermatitis: A Systematic Review and Network Meta-Analysis" published in JAMA Dermatology by Drucker et al. [30-31] to illustrate LSR production processes. Since the initial version development follows the same process as traditional systematic reviews, this section focuses on key aspects and processes of living updates.

5.1 Developing the LSR Protocol

Before initiating LSR production, the team registered the protocol "Systemic Immunomodulatory Treatments for Atopic Dermatitis: Protocol for a Systematic Review and Network Meta-Analysis" [32] on PROSPERO and published it in BMJ Open. In addition to conventional systematic review protocol content, the methods section added "Updating" content explicitly stating criteria for converting the systematic review to an LSR and for updates:

Research indicates that continuously updated living network meta-analyses can generate powerful, timely comparative effectiveness evidence [33]. The research question in this systematic review meets LSR update criteria: (1) The systematic review addresses a decision-making priority; (2) New information will change decision-making; (3) Relevant new studies are likely to emerge continuously. Therefore, if these criteria remain met at baseline review completion, the review will be converted to an LSR with network meta-analysis. Given the number of new systemic drugs for atopic dermatitis in development, this scenario is highly likely. We will conduct update searches monthly and add relevant studies to the review, with analyses updated at least every 4 months. However, update frequency will be higher if new studies meet any of three conditions: (1) Include data on new drugs not currently in the network meta-analysis; (2) Include comparisons between drugs never directly compared before; (3) Report results inconsistent with the latest network meta-analysis findings.

5.2 Literature Searching and Study Inclusion

After searching predetermined databases on October 28, 2019, the production team conducted update searches every 4 months, with iterative updates and retrospective searches in April 2021 to avoid missing eligible studies from previous versions. The team reported the number of added included studies on their official website (http://eczematherapies.com/research/) in October 2020, June 2021, and November 2022, providing basic characteristic tables, bias risk assessment results, and study findings.

5.3 Outcome Updates

After the first version was published in JAMA Dermatology, the research team published network plots and league tables for six outcomes on their website: patient-reported clinical sign improvement (EASI), symptom improvement (POEM), treatment discontinuation due to adverse events, serious adverse events, quality of life improvement (DLQI), and pruritus severity (PPNRS) (Figure 2 [Figure 2: see original paper]), with important outcome improvements published again in the journal in March 2022.

Conclusion

As a continuously updated systematic review methodology, LSRs improve traditional systematic review processes and evidence synthesis methods, continuously updating and synthesizing new evidence to provide decision-makers with timely, current information while greatly enhancing production efficiency and resource utilization. With continuous development of computer automation technology, many tasks in systematic review production can be completed through computer assistance. Through automated data collection, analysis, and synthesis, evidence can be updated more quickly and accurately, better addressing the constant emergence of new research. This means LSRs are poised to provide decision-makers with more high-quality evidence through computer-assisted technology, further advancing clinical practice and health fields. Additionally, computer assistance helps improve standardization and reproducibility of review processes, ensuring consistency and reliability of results. It is anticipated that LSRs will play an increasingly important role in helping decision-makers access high-quality, current evidence and contribute to improving clinical practice and health standards.

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