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Methods Corner

A practical guide to living evidence: reducing the knowledge-to-practice gap

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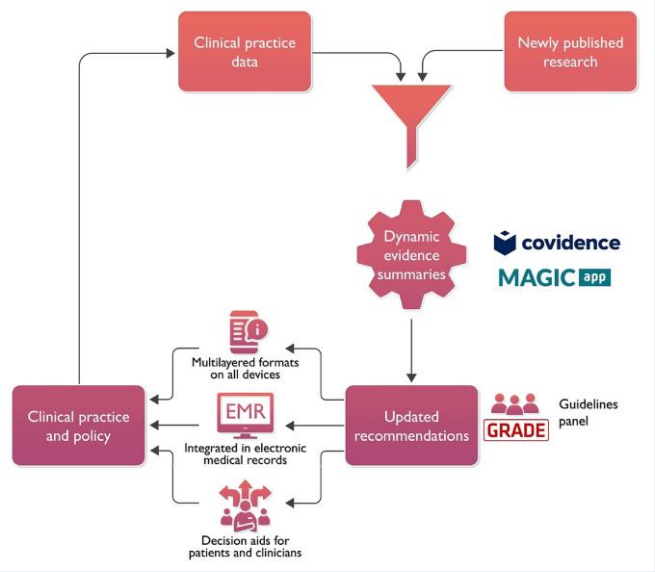
Living evidence involves continuous evidence surveillance to incorporate new relevant evidence into systematic reviews and clinical practice guideline recommendations as soon as it becomes available. Thus, living evidence may improve the timeliness of recommendation updates and reduce the knowledge-to-practice gap. When considering a living evidence model, several processes and practical aspects need to be explored. Some of these include identifying the need for a living evidence model, funding, governance structure, time, team skills and capabilities, frequency of updates, approval and endorsement, and publication and dissemination.

Graphical Abstract



Inspired by: https://strokefoundation.org.au/what-we-do/for-health-professionals/living-stroke-guidelines

Learning objectives
- Critique the current approach to producing evidence and clinical practice guidelines.
- Describe and understand living evidence.
- Review key considerations for living evidence including benefits, practicalities, challenges, and solutions.

The problem: currency of evidence

There remains a gap between what is known from the best available evidence and what is done in practice, described as the 'evidence-practice' or 'know-do' gap.[1] Despite advances to reduce the knowledge-to-practice gap,[2] it takes an average of 17 years for research evidence to reach clinical practice.[3] An essential component of the bridge between 'knowing' and 'doing' is the synthesis of complex, incomplete, and, at times, conflicting research findings into a format readily available to inform health decision-making.[2] Systematic reviews (SRs) and meta-analyses have been the long-standing contributors to this bridge in evidence-practice.[4] Although the methods of SRs and meta-analysis are well developed,[4–6] currency, a critical component of evidence accuracy, remains challenging. The time between the date of the last search to SR publication typically takes over 12 months,[7] and the time from primary study publication to incorporation in SR ranges from 2.5 to 6.5 years.[8] Furthermore, after publication, only a minority of reviews are updated within 2 years.[9] One study conducted an analysis to assess the period over which SRs remain up to date and found that the median 'survival' of SRs in the area of cardiovascular disease (CVD), which has a relatively high publication rate, was 2.9 years [95% confidence interval (CI) 1.1–5.3].[10] This means that SRs become out-of-date by 2–3 years after publication and may fail to incorporate new evidence that could substantially change the conclusions about the benefits or harms of therapies.[10]

Systematic reviews are the gold standard for informing clinical practice guideline recommendations.[11] Clinical practice guidelines are a key pillar of quality healthcare provision, providing evidence-based recommendations for clinicians and other healthcare professionals regarding the management for people with various health conditions.[12] It follows the three-circle model that highlights the importance of not only grounding clinical practice in high-quality science but also ensuring it reflects the clinician's role in deciding the best way to tailor the information to the specific needs and preferences of the patient.[13] The strength (i.e. strong and weak) and direction (i.e. in favour or against) of the recommendations are determined by the balance of benefits and harms as well as the quality of the supporting evidence.[14,15]

A guideline recommendation is as up-to-date as the search date of the supporting SR. In addition, guideline development or updates are time and resource intensive involving multiple experts and stakeholders. Previously the most common approach to updating recommendations is to update the entire guideline at specific time intervals e.g. 3- or 5 years following the last publication. However, this method poses some limitations that could negatively affect the validity of the recommendations and the efficiency of the guideline update process. It is likely that some of the recommendations will be outdated for varying periods affecting their validity while the efforts invested in the update of some recommendations will likely be wasted as the underlying evidence will not change. A study examining the validity of recommendations in clinical guidelines found that 92% (95% CI 86.9–97.0) of the recommendations were valid a year after their development or update.[16] This validity decreased to 85.7% at Year 2, 81.3% at Year 3, and 77.8% at Year 4.[16] Another challenge is that guidelines are often produced as peer-reviewed academic publications that remain static and immutable once published.[17]

A solution: 'living' evidence

Living evidence involves continuous evidence surveillance to enable timely updating of SRs and clinical practice guideline recommendations.[18] It supports rapid evidence synthesis without compromising the rigorous, gold-standard methods for conducting SRs or guideline development.

Key criteria for living evidence

When deciding to initiate a new or transitioning an SR or guideline recommendations into a 'living' one, review teams and guideline developers should ensure that all three of the following criteria applies[19]:

(1) Is the topic a high priority for decision-making? E.g. new adverse effects related to intervention requiring urgent changes to practice.
(2) Is there uncertainty in the existing evidence? E.g. a lack of high-quality reviews or gaps in aspects of the topic that are not covered by the existing evidence such as new interventions, subgroups, and outcomes?
(3) Is new evidence expected to emerge that is likely to change existing recommendations? E.g. ongoing trials, new trials in trial registries, or in-vitro studies which signals that a topic is actively researched.

Types of 'living' evidence

Living systematic reviews

'Living' SRs (LSRs) refer to the approach of updating in which SRs are updated as new research becomes available and relevant evidence is incorporated into the review.[20] The core review methods are not fundamentally different to traditional SRs. The only point of difference is how frequent new evidence is sought and screened and when it is incorporated into the review.[21]

Establishing and updating living systematic reviews

We summarized the challenges by steps in the lifecycle of an LSR and provided potential solutions to these challenges. *Table 1* outlines some innovative enablers that may help improve the efficiency of producing an LSR and its continual maintenance.

Setting up and managing a review team

The review team should include multidisciplinary members with varied capacities and skills, including experts who are familiar with traditional SR methods. There is a core team or an early-career researcher with skills and experience in evidence synthesis (depending on the size of the review) that coordinates the tasks of the review team, which includes distributing workload such as assigning roles among team members and setting expectations about responsibilities, managing workflow, and providing continual oversight of the process to ensure timelines are met.[23] The size of the review team is dependent on the search frequency and the estimated average monthly workload, which is determined by how many citations and newly included studies are expected to be found and how often the LSR will be updated, i.e. a new version published.

Challenges: Increase in the number of citations to be screened can become overwhelming. As such, it is common for

Table 1 Living systematic review tools (adapted from Thomas *et al.*[20] and Elliot *et al.*[22])

Review task	Tools
Setting up and managing a review team	**Cochrane Crowd** is a citizen science platform made up of a global community of volunteers from the general public who help review descriptions of research studies to identify and classify clinical trials. This helps Cochrane reviewers and other healthcare researchers around the world find high-quality evidence about treatments and other healthcare interventions (https://crowd.cochrane.org/). **Cochrane Engage** is a platform that connects reviewers who need help with their Cochrane reviews with people who have the time and expertise to help. Authors post requests for help with aspects of a review, for example screening, translation, or data extraction (https://engage.cochrane.org/).
Study identification	Automated email alerts (auto-alerts) of new results for saved searches within bibliographic databases. Notification from clinical trial registries **Epistemonikos** is a database of all of the evidence relevant for health decision-making, including world's largest SR database, curated, and annotated by a network of collaborators (http://epistemonikos.org). **Health Databases Advanced Search (HDAS)**—National Institute for Health and Care Excellence (NICE) Evidence Service's healthcare databases advanced search (HDAS) enables you to search across one or more of our eight databases—AMED, BNI, CINAHL, Embase, Health Business Elite, HMIC, Medline, and PsycInfo. You can search individual databases or some or all at the same time (http://hdas.nice.org.uk/).
Study selection—Workflow management	**Covidence** is a software for managing and streamlining SRs that enables the whole review team to collaborate from anywhere (https://www.covidence.org/). **Evidence for Policy and Practice Information (EPPI)-Reviewer** is a web-based software programme for managing and analysing data in literature reviews including SR, meta-analyses, 'narrative' reviews, and meta-ethnographies (https://eppi.ioe.ac.uk/cms/Default.aspx?tabid=2914). **Rayyan** is an artificial intelligence (AI) powered tool for SRs. It helps expedite title/abstract screening using a semi-automation process (http://rayyan.qcri.org/). **Open-source software** is a software developed and maintained via open collaboration, and made available, typically at no cost, for anyone to use, examine, alter, and redistribute, e.g. R Shiny, open-source R package that enables web framework for building web applications.
Study selection—Screening studies	**Screen4me** is a service designed to help review teams with screening of search results much more quickly without compromising on quality. It is made up of: *Known assessments*—records go through Cochrane Crowd and receive a final classification of either describing a RCT or not. *RCT classifier*—a machine learning tool that distinguishes between RCTs from non-RCTs by assigning a likelihood score. *Cochrane Crowd—citizen science platform* (https://training.cochrane.org/online-learning/good-practice-resources-cochrane-authors/screen4me).
Study selection—Retrieving full-text papers	**CrossRef API** allows searching, filtering, or sampling research metadata making them easier to find, cite, link, assess, and reuse (http://search.crossref.org/).
Data extraction and quality assessment	Machine learning and automated structured data extraction tools collect information about PICO components and/or risk of bias RobotReviewer (https://www.robotreviewer.net/) Research Electronic Data Capture (REDCap), Microsoft Forms, Qualtrics, and other online forms to create data extraction forms and distribute as a survey to review teams.
Data synthesis	**RevMan HAL** generates text for most sections of the abstract, summary of search, effects of interventions, and summary of main results in discussion. Plans for next version include using data from the title, an editable repository of text containing information about scales and treatments, and information from the data and analysis table to automatically generate text to include in the description of conditions and interventions of the background and references and text to be included in the outcome scales section of the results.

review teams to increase the size of the team to help with screening and data extraction. However, finding and forming a diverse group of contributors with capacity and skills can be challenging.

Solutions: Crowdsourcing or citizen science (the process of aggregating crowd wisdom or involving members of the general public in scientific research) and task-sharing platforms are valuable tools for large reviews.[22] Training must be provided by the core team to reduce

potential disagreements in screening and delays in completion of the LSR. Therefore, the core team must evaluate the time spent on training crowd-sourced volunteers against the time saved. Training can be provided using pre-recorded videos uploaded into the platform being used. When using crowd-sourced members or citizen science, it is critical the core team defines the eligibility criteria for authorship right at the beginning. Team members who fulfil the authorship criteria should be included as co-authors and those who do not should have their contributions acknowledged.[24]

Publishing a protocol

An LSR protocol is also a living document that is updated as review questions and scope and types of included evidence change over time.[20] Prior to starting an LSR update, any changes to the protocol should be documented and justified including decisions about the frequency of updates as well as stopping the review.[25] Registration of a protocol in PROSPERO (https://www.crd.york.ac.uk/prospero/) or on public repositories such as Open Science Framework (https://osf.io/) allows for rapid sharing and updating of protocols. Cochrane has processes around proposing or registering a new Cochrane review or transitioning an existing one to living mode.[21] In addition to the traditional SR protocol information, LSR protocols also contain details around the search methods and frequency, deciding when to integrate new information, e.g. new studies and development of new interventions, and deciding when an LSR should be transitioned out of living mode.[21]

Baseline review

The baseline review is either an entirely new review for a new LSR topic or an updated version of an existing one. Once the baseline review is published, only after this point will the 'living' part of the LSR commence.[21]

Study identification

Identification of studies for inclusion involves searching electronic bibliographic databases, downloading the results, uploading them into citation management software, and deduplicating records. Access to an information specialist who can run and manage the search and maintain the search strategy may be available to Cochrane-registered LSRs.

Challenge: The study identification process is even more labour-intensive and time-consuming with LSRs as the searches are conducted more frequently.

Solutions: There are a number of ways to streamline the database searching process. Many bibliographic databases support an automated email alert system (auto-alert) when new results are available for saved searches.[22] If a member of the core team has sufficient programming skills, setting up automatic transcripts to regularly search and download results from databases using an open application programme interface (API) can also be done.[23] Database aggregators such as Epistemonikos database and the Health Database Advanced Search (HDAS) offer the potential for regular comprehensive searches by allowing users to search multiple databases simultaneously.[22,23] In the case where a relevant database is not supported by the aforementioned services, manual searching has to be conducted. This task can be distributed to multiple individuals in the review team where each is responsible for one or two databases.

Study selection

Potentially relevant studies identified from database searching and other sources need to be checked against the eligibility criteria of the LSR.

Challenges: Establishing mechanisms for collaboration among team members and ensuring a secure and efficient workflow during the study selection process can be challenging. In addition, the volume of citations that need to be screened manually and the number of studies to be retrieved for final selection and inclusion place a huge burden on reviewers.

Solutions: There are several fast and user-friendly platforms that organize and facilitate the screening of records for LSRs.[26] These includes Covidence,[27] Evidence for Policy and Practice Information (EPPI)-Reviewer,[28] and Rayyan.[29] They support multiple users, delegate tasks, record decisions (include or exclude), and produce automatic reports. However, these tools have a user fee based on a subscription model. Most universities and research institutions have a subscription available for staff members to use. In instances where these software tools are unaffordable, it is possible to build a custom application using open-source software such as R Shiny.[23]

A number of semi-automated machine learning tools can reduce the volume of studies manually screened for LSRs.[30] These includes machine learning classifiers, e.g. randomized controlled trial (RCT) classifiers and text classifications, crowdsourcing, e.g. Cochrane Crowd, and integrated systems, e.g. Screen4me.[21,22] Machine learning classifiers need to be trained with large amounts of high-quality data to be able to be very accurate in predicting that a new citation is describing an RCT.[31] A study by Wallace *et al.*[31] found that RCT classifiers is able to exclude 60–80% of irrelevant records from a database search while maintaining a 99% sensitivity rate. Platforms such as Rayyan also use artificial intelligence to calculate the likelihood of each article to be included by producing a five-star rating.[29]

Services such as CrossRef API can be used to automate the discovery of full-text papers.[21] However, it still requires human effort and judgement to track down all papers and navigate subscription permissions.

Data extraction and risk of bias assessment

This is the stage where information from all included studies such as study characteristics and results data are extracted in a standardized manner and assessment of how the study has been conducted; i.e. risk of bias is performed.

Challenge: Secure, independent, and efficient data extraction by reviewers and management of huge volume of data by the core team.

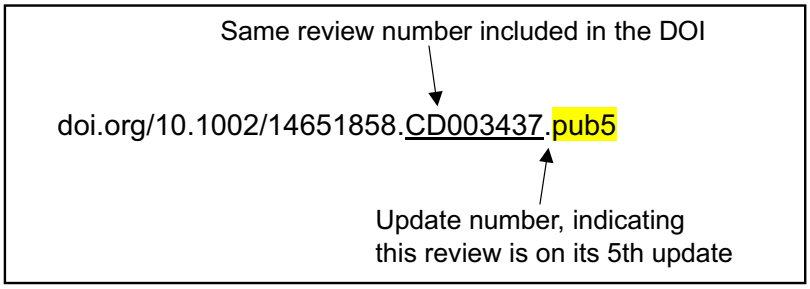
Solutions: There are a number of machine learning and automated structured data extraction tools, but very few are publicly available and have limitations around adaptability to a topic area on which the tool was not developed for to begin with. In Covidence, there is an option to develop your own data extraction form or utilize the available template.[27] Data extraction forms can also be created and distributed using Research Electronic Data Capture (REDCap),[30] Microsoft Forms,[32] Qualtrics,[33] and other online forms. Risk of bias assessment can also be partially automated using machine learning tools such as RobotReviewer.[34] Reviewers have considered the option of using this technology to replace one human reviewer, which may reduce the workload. However, outputs still need to be manually verified, and as with any machine learning tools, it has to be trained to accurately apply the critical appraisal tool.[22]

Data synthesis

Prior to data synthesis, extracted data need to be checked particularly when crowd members have contributed to the selection and extraction of data. An important step in data synthesis is the thoughtful consideration of whether it is appropriate to combine the numerical results of all or some of the studies. Chapter 10 of the Cochrane Handbook outlines how to undertake meta-analyses.[35]

Challenge: Incorporation of new studies in the appropriate analyses and generating/updating sections of the review based on new findings remains difficult. Issues associated with repeated updating of statistical analysis and inaccurate estimation of heterogeneity across studies may arise as more updates are performed.[36]

Box 1 Cochrane indexing system



Solutions: Automation technologies for data synthesis are still in the early stages. However, technologies such as RevMan HAL and RevMan Replicant, which generate sections of a review based on templates and quantitative findings, exist.[21,22] Living SR teams have also used API to connect an online database and statistical software to import the latest data and update the analysis when new data are available.[23] It may be as simple as creating reproducible documents, tables, and/or figures to quickly update results when new studies are included.

Prior to starting or updating an LSR, select review team members with statistical expertise who are familiar with employing methods to avoid statistical problems when updating meta-analyses.[36]

Publishing

Publication formats that can be updated frequently are a requirement when disseminating LSR outputs. Transparency is also critical when sharing the results of LSRs.

Challenges: Different versions of LSRs are often mistaken for redundant publications. Maximizing the value, the LSR provides to end users at all times.

Solutions: LSRs should be published in a way that explicitly cross-references different versions as updates of the same review. Contacting the target journal editor is the best way to determine whether the journal is accepting LSR submissions in the first instance and how they handle updates. How editors consider a 'version of record'[37] [a version of an article that is considered final and is assigned a digital object identifier (DOI)] varies across journals. Cochrane has used an indexing system for updates for many years and assigns a DOI that includes the same review number for all updates and an extension with the update number.[21] See the example in *Box 1*. Cochrane also alerts readers when they are not viewing the most recent version and provides a link to the current version. Readers also have access to the version history of the review.[21] Online publishers such as F1000 also use a similar versioning principle as Cochrane.[38] The BMJ and Annals of Internal Medicine also support frequent updating of LSRs.

Having some possible update scenarios documented in the protocol prior to starting an LSR is recommended.[21] Cochrane has a system that informs readers about the currency of LSRs based on update scenarios. A 'What's new events' table provides a status update, the date of the last search, and describes changes between the previous version including whether or not new additional evidence was identified and changed the conclusion of the review.[21] See the example in *Box 2*.

Stopping living systematic reviews

In addition to the frequency of updates, when to stop is another important feature of LSR. The criteria for stopping should be documented in the protocol and updated as necessary.[21] Some review teams allocate a specific date at which they intend to stop while others consider the three key criteria for a living approach outlined above: new evidence is unlikely to emerge, the question is no longer of importance, and the effect estimates are stable.[19]

Living guidelines

A living guideline is evidence based and comprises one or more living recommendations that are rapidly updated as new evidence becomes available.[19] It identifies and provides a justification for which recommendations are living or static and include a rationale for the planned updating frequency.[19] Prioritization of recommendations to switch to the living status is imperative in order to maximize the value of the approach. Refer to the key criteria for living evidence above.

Criteria for frequency of searches or update of recommendations

The following are criteria for considerations when making decisions about the frequency of searches or updating of recommendations[17]:

(1) How urgently does the topic require updated recommendations?
(2) How fast is the new evidence emerging?
(3) What are the resources and costs for the continual development and/or updating of recommendations?

A clear, *a priori* description of the methods that are followed to make decisions about the frequency of or thresholds for incorporation of new research into evidence profiles and publication of updates to the recommendations should be documented.[17]

Elements necessary for producing living recommendations in guidelines

Living systematic reviews. Refer to LSR section above. Collaboration between the LSR and living guideline teams is critical. A smooth workflow will require coordination and integration of work processes including the tools and platforms used.

Living summary tables. Updating the standardized summary tables as soon as new evidence is available ensures that the findings of the LSR are relayed quickly to guideline panels allowing them to reconsider the recommendation. This process is facilitated by MAGICapp, a web-based collaborative tool that does not require any software installation and allows publication on all devices.[39] Guideline developers can write and publish their guidelines and evidence summaries, in compliance with guideline development standards using the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) methodology (refer to section 7 supporting information technology), novel technology, and a variety of developed frameworks. It allows guideline admins, authors, technical team, and systematic reviewers to work together on the content.[40] Any changes to the content can be seen by all, and there is an activity log to ensure transparency.[40]

Box 2 Ongoing monthly searches have identified new evidence that is likely to change the review conclusions (adapted from Cochrane LSR Guidance[21])

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 search results to 27 April 2019 (two new studies and three new ongoing studies), is due in July 2019. As of the last search (27 June 2019), there are also two additional new studies to be included after the July 2019 update and four new ongoing studies.

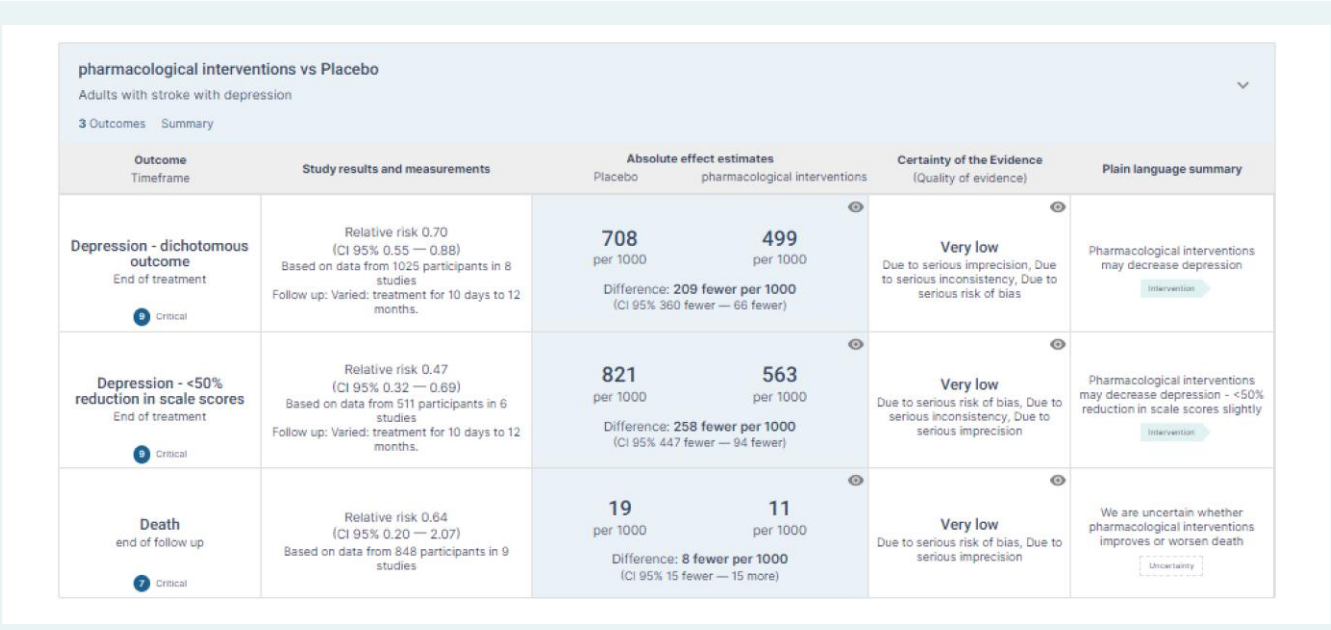


Figure 1 Example of evidence profile for pharmacological interventions for post-stroke depression—Chapter 6 of 8, managing complications: mood (https://informme.org.au/guidelines/living-clinical-guidelines-for-stroke-management). Adapted with copyright permission from the National Stroke Foundation of Australia.

Permissions can be set to ensure team members only have access to allocated content.[40] There are two types of tables:

- **Living evidence profile**: a table that contains the statistical information on the effects (benefits or harms) of alternative interventions and assessment of the certainty of supporting evidence for each outcome of interest.[41,42] *Figure 1* shows an example of an Evidence Profile taken from the Australian National Stroke Foundation living guidelines developed and published through the MAGIC authoring and publication platform (MAGICapp).
- **Living evidence to decision:** a table that outlines the information on factors such as the effects (benefits and harms) of interventions, certainty of evidence, values and preferences, and resource use needed to judge the strength and direction of the recommendation.[14,43] *Figure 2* shows an example of an evidence to decision table taken from Australian National Stroke Foundation living guidelines developed and published through MAGICapp.

Living guideline panel. Recruiting panel members with appropriate evidence-based methods, information management training, and links to relevant professional and consumer organizations who understand the time commitment and rapid responses required, ahead of time is crucial.[17] Virtual meetings would be more feasible in this instance.

Living peer review process. This involves the recruitment of a larger number of reviewers committed to ensuring a timely review.[17] Reviewers are notified as soon as the updating process is triggered. Creating a clear, explicit, and adaptable governance framework will help streamline evidence assessment and recommendation update workflows.[19] Careful planning and inclusion of any internal or external review and endorsement processes as well as periods of public comments in the guideline timeline are essential.[19]

Living publication and dissemination. Living guidelines also face similar challenges related to publication and dissemination like LSRs.[20] These include ensuring that the latest version of the recommendation can be clearly identified, and historical information (living summary tables) related to the previous versions of the recommendation can be accessed as well as challenges related to authorship indexing and versioning if published in journal article form.[22] In terms of dissemination, the key challenge would be ensuring that any change in recommendation is reflected in real time and target users are made aware of this change. Refer to *Figure 3* for example of how changes to recommendations are noted in MAGICapp. Through MAGICapp living guidelines are linked to information systems at point of care, e.g. electronic medical record and decision support tools.[40] This would mean that any changes to a living guideline recommendation would be reflected in the online living

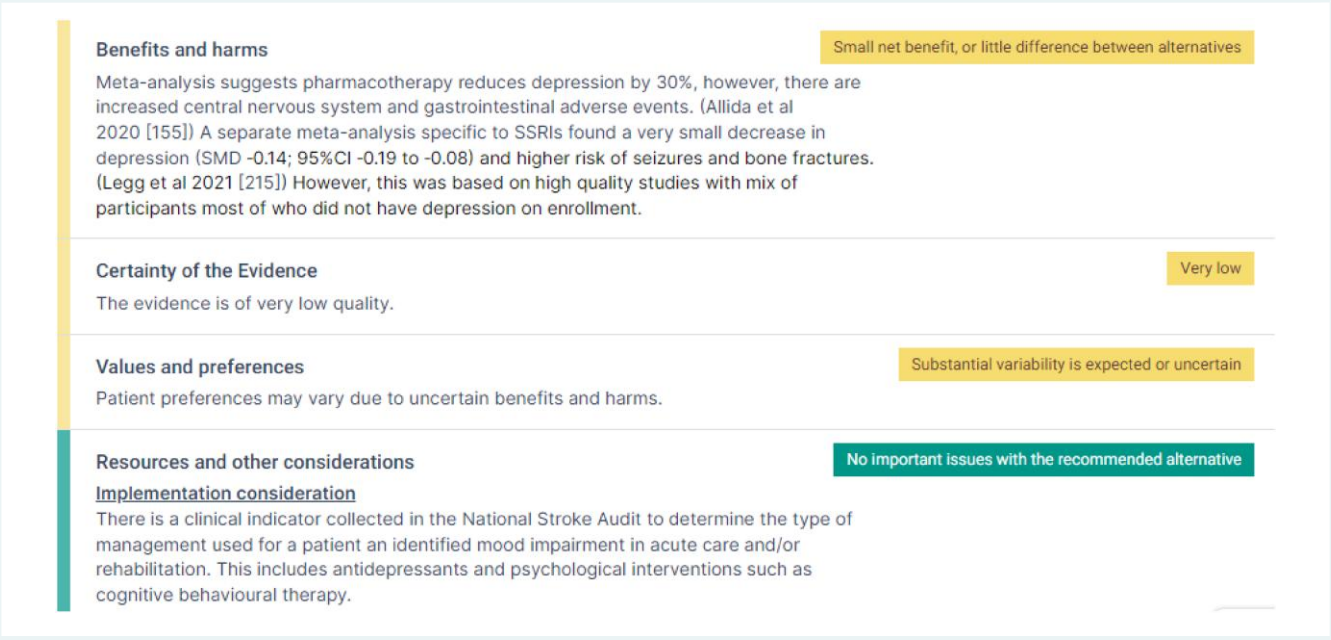


Figure 2 Example of evidence to decision table for pharmacological interventions for post-stroke depression—Chapter 6 of 8, managing complications: mood (https://informme.org.au/guidelines/living-clinical-guidelines-for-stroke-management). Adapted with copyright permission from the National Stroke Foundation of Australia.

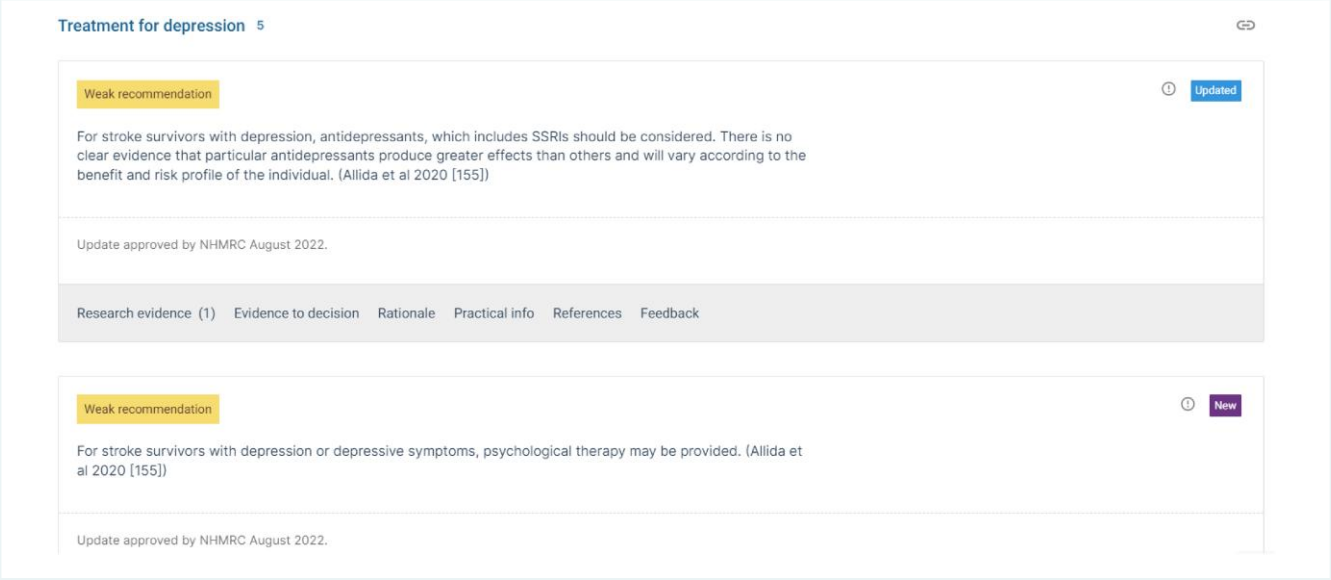


Figure 3 Example of how changes to recommendations are noted in MAGClapp—Chapter 6 of 8, managing complications: mood (https://informme.org.au/guidelines/living-clinical-guidelines-for-stroke-management). Adapted with copyright permission from the National Stroke Foundation of Australia.

guideline document and linked systems.[12] Once published, content can also be exported as pdf or Word. Decision aids are automatically produced from the content in a multi-layered presentation that displays components of the GRADE assessments, including the list of patient important outcomes, confidence in estimates, burden of treatment, and cost.[2]

Living budget. Having sufficient start-up funding for the initial living mode period is essential. Living guidelines often start off as a pilot programme and evolve into a mature one with longer-term support.[19] The amount of funding required is dependent on the scope, volume, and complexity of evidence to be reviewed, governance structures, resources, access to software platforms and licensing costs, and dissemination.[19] A modelling conducted by the Australian National Stroke Foundation found that the cost of updating the living stroke guidelines is similar to updating guidelines on a 5-year cycle.[44] An ongoing funding commitment is critical to ensure the medium to long term sustainability

Table 2 World Health Organization COVID-19 therapeutics living guideline example of the practicalities[44]

Practicalities	Application in the WHO COVID-19 therapeutics living guideline[a]
Funding	Bill & Melinda Gates Foundation, Norwegian Directorate of Public Health, and Germany
Governance structure	*WHO Therapeutics Steering Committee* responsible for determining the availability of sufficient evidence to trigger guideline updates and convening the Guideline Development Group *WHO rapid review team* responsible for evidence updates reviewed by the Steering Committee *Guideline Development Group* evaluates the drug by considering individual patient perspective, resource implications, acceptability, feasibility, equity, and human rights. *Guideline Support Collaboration Committee* provides the coordination between WHO and MAGIC to allow the rapid development of the guideline and its dissemination into various publication platforms.
Team	*WHO Therapeutics Steering Committee* consists of representatives from various WHO departments at headquarters and the regions and has been approved by the WHO Director of the Country Readiness Department, and the WHO Chief Scientist *WHO rapid review team* *Guideline Development Group* includes clinicians and research experts *Guideline Support Collaboration Committee*
Frequency of updates	As frequently as needed
Supportive IT	GRADE[42] and MAGICapp[39]
Approval and endorsement	Drafts circulated to external reviewers. All comments were reviewed and responded to by the relevant Guideline Development Groups with final discussion and sign off by the steering committee.
Publication and dissemination	The living guideline is written, disseminated, and updated in an online platform (MAGICapp), with a user-friendly format and easy-to-navigate structure that accommodates dynamically updated evidence and recommendations, focusing on what is new while keeping existing recommendations updated within the guideline. The current guideline and its earlier versions are available through the WHO website, the British Medical Journal, and MAGICapp (online and also as PDF outputs for readers with limited internet access).

[a]https://www.who.int/publications/i/item/WHO-2019-nCoV-clinical-2023.2.

of living evidence projects. Sustainability can be challenging without the ongoing support of government funding.

Supporting information technology. **MAGICapp** has a licence subscription model. For organizations to start to develop and publish guidelines, an administration account must be set up first (https://magicevidence.org/magicapp).

GRADE is a transparent framework for developing and presenting summaries of evidence and provides a systematic approach for making clinical practice recommendations. It has four domains that include risk of bias, imprecision, inconsistency, indirectness, and publication bias. Authors can lower the certainty of evidence by one or two levels, e.g. from high to moderate to low to very low. GRADEpro GDT (https://www.gradepro.org/) is the tool used to create summary of findings tables for Cochrane reviews. GRADEpro integration can be enabled to link GRADEpro with RevMan. This means that questions and outcomes can be imported from RevMan, evidence grading, and certainty calculation can be done in GRADEpro, and summary of findings tables will be created automatically in your review. Access is free for groups of up to three researchers. Teams working on <3 projects at a time and organizations managing multiple guideline projects have to pay a subscription fee.

Example 1: World Health Organization (WHO) Therapeutics and COVID-19 Living Guideline

The WHO Therapeutics and COVID-19 living guideline incorporates new evidence to dynamically update recommendations for COVID-19 therapeutics.[45] This is related to the larger, more comprehensive guideline for COVID-19 clinical management. The COVID-19 pandemic—and the explosion of both research and misinformation—has highlighted the need for trustworthy, accessible, and regularly updated living guidance to place emerging findings into context and provide clear recommendations for clinical practice. This living guideline responds to emerging evidence from RCTs on existing and new drug treatments for COVID-19. The processes and practical aspects of the WHO Therapeutics and COVID-19 living guideline are detailed in *Table 2*.

Example 2: Australian Stroke Living Guidelines

Living guidelines are not limited to communicable diseases; they can also work for non-communicable diseases such as CVD or stroke. Take the Australian Stroke Living Guidelines as an example. In 2017, the Australian National Stroke Foundation released the last static/periodic update of the Clinical Guidelines for Stroke Management, which consisted of 392 individual recommendations across eight chapters addressing 89 topics.[46,47] The Stroke Foundation in collaboration with Cochrane Australia was awarded 3 years of funding from the Australian Government to test a living model of the stroke guidelines. At the time, these were the first Australian living clinical guidelines and the first and only living stroke guidelines, globally. The living stroke guidelines are developed based on the National Health and Medical Research Council standards for evidence-based guidelines, using MAGICapp,[39] which incorporates the GRADE method for recommendations.[48] The practical aspects of the living stroke guidelines are detailed in *Table 3*.

What are the benefits of living evidence?

One of the main benefits of living evidence is that it enables research innovation. Scientific progress is dependent on the ability of researchers

Table 3 Australian living stroke guidelines example of the practicalities of transitioning a static guideline to a living mode

Practicalities	Application in the Stroke Foundation living guidelines[a]
Funding	Australian Government Medical Research Future Fund over 3 years
Governance structure[45]	*Project Executive Group* responsible for project oversight. *Guidelines Content Development Group* responsible for content development. *Content Steering Committee* took overall responsibility for content development and signing- off new and changed recommendations. *Guideline Delivery Team* responsible for programme coordination and evidence support
Team[45]	*Project Executive Group* consists of senior members of the Stroke Foundation and Cochrane Australia, and the co-chairs of the Guidelines Content Development Group *Guidelines Content Development Group* comprises 11 working groups (acute medical, rehabilitation-medical, nursing, physiotherapy, occupational therapy, speech pathology, psychology, dietetics, other disciplines, health economics, New Zealand (NZ) representatives, and a consumer panel). Each topic had small writing group consists of clinical experts (2–5 members) and consumers with lived experience (2–3 members). *Content Steering Committee* consists of the leads from each working group, along with two co-chairs and a NZ representative *Guideline Delivery Team*
Frequency of updates	Every 6 months or more frequently as needed.
Supportive IT	Covidence,[27] GRADE,[42] and MAGICapp[39]
Approval and endorsement[45]	Draft changes were circulated via email and social media to all stakeholder groups for comment over a 4- to 8-week period. All comments were reviewed and responded to by the relevant working groups with final discussion and sign off by the steering committee followed by submission to the National Health and Medical Research Council for approval.
Publication and dissemination[45]	Monthly updates to the guidelines were disseminated through email distribution to over 18 000 health professionals and students. Specific changes were also shared via website postings and social media channels. Changes to recommendations were noted directly in MAGICapp, with specific labels for 'Updated' or 'New' as appropriate. Refer to *Figure 3*.

[a]https://informme.org.au/guidelines/living-clinical-guidelines-for-stroke-management.

to connect distinct and cross-disciplinary ideas.[49] With the ever-increasing volume and complexity of literature, improved processes are essential to facilitate the connection of researchers with a broad range of knowledge. Living evidence can support this by providing concise, reliable, and current knowledge, highlighting critical knowledge gaps, identifying claims in need of replication, and proposing new combination of topics.[49]

Another benefit of living evidence is that it supports effective knowledge translation by creating an opportunity for active partnerships between researchers, non-government organizations, policymakers, and consumers.[2] By doing so, it has the potential to yield significant economic benefits by improving patient outcomes and efficiency of expenditure on healthcare and services. Improving the currency and reliability of clinical guidelines through a living model will help identify high and low value care as well as previously accepted treatments that no longer provide net benefit more rapidly, enabling disinvestment in outdated or ineffective treatments and investment in newer or more effective treatments.[50]

An economic modelling of the potential impact of 'living' vs. conventional updating of guideline recommendations within the first year of practice-changing evidence becoming available for two interventions: (i) nurse-led intervention for managing fever, hyperglycaemia, and swallowing after stroke (FeSS protocol)[51] and (ii) addition of a new class of drug, sodium glucose co-transporter 2 inhibitors to the current management standard for people with Type 2 diabetes and CVD[52] was conducted. They found that the net social benefit delivered by living guidelines in these two case studies was AU$292 million (AU$1107 per affected person) and AU$944.2 million (AU$13 584 per affected person), respectively.[53]

Finally, living evidence also creates a novel opportunity for early-career funding. With the ever-increasing competitiveness of grant applications and lesser funding awarded to early-career researchers, a knowledge synthesis grant would be an ideal first funding and foundation for them to grow their knowledge domain, build recognition, identify research programmes, promote capacity-building, and create well-justified project proposals that would make them competitive for further funding.[54]

Outlook for living evidence in cardiovascular disease

In a modern healthcare system, timely evidence assessment, synthesis, and clinical recommendations are critical to reduce the knowledge to practice lag and help minimize the evidence-practice gap. It should no longer be acceptable for evidence to be out of date and researchers and funders have the responsibility to ensure trustworthy and up-to-date evidence is available to guide health decision-making and prevent investment waste. 'Living' evidence is a contemporary method that can address this issue by enabling timely update of clinical practice recommendations and support timely uptake of new evidence to practice. Living evidence is a core element of a learning health systems model that strives for continuous practice improvement.[55,56]

Although the living evidence model has been around for 8 years, the digital technologies, platforms, and processes that support them are relatively new and there is still much to learn. We can certainly learn from colleagues working in the cancer specialty who have been an early adopter of wiki-based platforms to ensure speedy recommendation update.[57] In 2011, the Australasian Sarcoma Study Group and Cancer Council Australia modified and customized an open-source Wiki software application—MediaWiki[58] to translate the guideline development process into an online environment. This provided them with an iterative and constantly updating framework where infrastructure is in place for automatic literature updates from PubMed and Embase to relevant question authors as well as manual submission of new or emerging evidence by experts at any time using the comment and submit new evidence function embedded within each research question page.[59] As a result, the guidelines reflect the most up-to-date evidence base. Key learnings from this methodology and processes are beneficial and can be applied for other scientific fields, particularly CVD.

Critical to implementing a sustainable living evidence model is having efficient mechanisms for sharing of data between groups undertaking evidence synthesis locally and internationally—either to conduct LSRs or produce living guidelines. Cochrane is currently exploring the potential for linked data (https://linkeddata.cochrane.org/) to enable systems to interchange and share data more efficiently. There is also growing openness for trial data to be included in an individual participant data repository.[60] Furthermore, it is also important to articulate the value proposition of living evidence, so consumers, end-users, and funders have a clear understanding of the potential for long-term impact and the resources required for implementation at scale and sustainability. More research that closely examines complex clinician behaviour change through the adoption of guidelines and use of registry and audit data in practice and ultimately how this contributes to improved patient outcomes is also needed.

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Data availability

No new data were generated or analysed for this article.

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