Australian
Living Evidence
Collaboration

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The Living Guidelines Handbook

Guidance for the production and publication of living clinical practice guidelines

Version 1.1

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The Australian Living Evidence Collaboration is a partnership of leading clinical, consumer and research groups in stroke, diabetes, heart disease, kidney disease, musculoskeletal conditions, COVID-19 and cancer. The Collaboration is led by Cochrane Australia (based in the School of Public Health and Preventive Medicine at Monash University).

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Australian Living Evidence Collaboration - Living guidelines:

- **Stroke** Living Guidelines: Stroke Foundation (2022). Clinical Guidelines for Stroke Management. Melbourne Australia. https://informme.org.au/guidelines/clinical-guidelines-for-stroke-management#

- **COVID-19** Living Guidelines: National COVID-19 Clinical Evidence Taskforce. (2022 version 57). Australian guidelines for the clinical care of people with COVID-19. https://livingevidence.org.au/living-guidelines/covid-19/

- **Kidney Health** Living Guidelines: Walker R, Palmer S, Tunnicliffe DJ, Cashmore B, Kostner K, Krishnasamy R, et al. Management of cholesterol-lowering therapy for people with chronic kidney disease. CARI Guidelines. Sydney, Australia; 2021. https://app.magicapp.org/#/guideline/7196

- **Arthritis** Living Guidelines: Australia and New Zealand Musculoskeletal Clinical Trials Network (2022 version 1.15). An Australian Living guideline for the Pharmacological Management of Inflammatory Arthritis. https://app.magicapp.org/#/guideline/LqRV3n

- **Diabetes** Living Guidelines: Living Evidence for Diabetes Consortium. Australian Evidence-Based Clinical Guidelines for Diabetes 2020. Melbourne, Australia. https://app.magicapp.org/#/guideline/7844

Disclaimer

This guidance is a "living" document and will be updated and expanded as methods are further developed and refined.
Currently, this is version 1.1
New sections are highlighted and marked as "**NEW**" or "UPDATED".
For a complete description of the changes, please see the changelog below.

Changelog

The first draft of this Handbook was developed in July 2021 and nine subsequent revisions were made leading to publication of Version 1.0

Version 1.1 Changes were not of a substantial nature: updating the ALEC logo, rectifying broken links, resolving formatting issues, fixing some minor errors.

Contents

1 Introduction

The purpose of this Handbook is to describe the methods and processes for developing living guidelines in healthcare. The handbook primarily aims to support guideline developers, including authors, information specialists, researchers, consumers, panellists, and other stakeholders in the living guidelines development process.

1.1 How to use this handbook

The handbook is presented in sections reflecting each stage of the guideline development process. The sections are presented as step-by-step stages but due to the living nature of the process, many steps will be nonsequential. Also, not all sections will be applicable to all guidelines. The handbook is modelled on our experiences developing living guidelines for major chronic health conditions and COVID-19 management within the Australian Living Evidence Collaboration (ALEC).

1.2 Types of living guidelines

There are two types of living guidelines that are referred to throughout this handbook:

- "*De novo*" living guidelines: guidelines that are established using a living approach
- Transitioned living guidelines: pre-existing guidelines developed using traditional methods where the whole or parts of the guideline are transitioned into living mode.

1.3 What this handbook covers

This handbook provides advice for guideline developers on how to construct living guidelines by illustrating the key differences needed to develop a living guideline compared to a traditional guideline. The handbook is not intended to be prescriptive but aims to capture the variety of approaches that can make successful and sustainable living guidelines.

1.4 What this handbook does not cover

This handbook does not replace guidance for the development of traditional evidence-based guidelines. Living approaches to guideline development assume that all the standard methods for the development of evidence-based guidelines still apply. For this please refer to guidance on developing evidence-based guidelines established by your local authorities, such as the Australian National Health and Medical Research Council (NHMRC)(1), Guidelines for Guidelines Handbook, the National Institute of Health and Care Excellence (NICE)(2), the Scottish Intercollegiate Guidelines Network (SIGN)(3), the Institute of Medicine (IOM)(4) or the World Health Organization (WHO)(5).

1.5 Principles for ALEC living guidelines

Commitment to rigorous evidence-based methods

All ALEC living guidelines are developed using methods designed to meet the NHMRC Standards for Guidelines.

Frequency of search/incorporation/publication

For all living recommendations, ALEC living guidelines:

- undertake systematic searches for new research evidence once every three months; and
- provide updates to users on new evidence identified and plans for inclusion once every three months; and
- provide a clear, *a priori* description of the methods that are followed to make decisions about frequency of or thresholds for incorporation of new research into evidence profiles, and publication of updates to the recommendations.

2 What are living guidelines?

Living guidelines are an innovative approach to ensuring that clinicians always have access to up-to-date evidence-based guidance to support decision-making. They are part of a suite of prospective and living approaches to evidence synthesis and have been called "the way of the future" for providing clinical guidance. (6,7)

In their seminal paper, Akl et al.(7)(8) described living clinical practice guidelines as an "optimisation in the development process" that allows updating of individual recommendations as soon as new evidence is available, which they highlight comes from living systematic reviews (LSRs). This definition points to the key element of updating "as soon as available" and the reliance on LSRs to underpin living recommendations. Based on this description, we propose the following definition, which acknowledges there are additional aspects to living guidelines, beyond the sole dependency on LSRs.

2.1 Definition of a living guideline

A living guideline is an evidence-based guideline that comprises one or more living recommendations that are continually updated as new information becomes available.
Living guidelines identify and provide a justification for which recommendations are living or static and include a rationale for the planned updating frequency.

What this definition means

We adhere to the definition of "clinical practice guideline" stated by the IOM (9). In this definition, building on Akl et al.(7), and based on our experience within ALEC, we acknowledge there is a spectrum of living guideline processes and methods that go beyond the conduct of an LSR.

For instance, a living guideline may contain recommendations transitioned from an existing guideline, as opposed to being initially developed in living mode. It may also include some recommendations that are living and others that are not. Lastly, living recommendations rely on continual evidence surveillance, but they may not necessarily include all the components of an LSR. For example, a living guideline may include systematic reviews produced by others, rather than conducted by the internal developing team. This definition acknowledges that the outcomes at each step of the guideline development process and indeed the process as well can be updated. Living guidelines enable rapid production of guidance without compromising the rigorous, gold standard methods for guideline development.

2.2 How do living guidelines differ from other approaches to updating guidelines

The key concept underpinning living guidelines is continual evidence surveillance and updating of recommendations. This is reflected primarily in:

- the increased frequency of searching,
- the study identification and selection, and
- the incorporation of new evidence and new recommendations into the guideline
- and publishing an update.

There are no fixed time intervals for searches or frequency recommendations should be developed or updated depending on several criteria including:

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

The guideline-developing team may opt for daily, weekly, monthly, or quarterly evidence surveillance. Also, evidence searches/updates may be conducted at different frequencies for different recommendations within the guideline.

The frequency of panel meetings to consider new evidence and updated recommendations may also vary from weekly, monthly, quarterly or ad hoc (depending on when new evidence emerges).

Although there is not an established maximum period for new evidence searches or recommendation updates for a guideline to be considered living, the following are considered the current "standard":

- an evidence search frequency of once every three (3) months*
- consideration and publication of updated recommendations once every six (6) months[1]

We are aware that there may be circumstances where this frequency is not possible or may be varied. This updating frequency is the fundamental difference from traditional guideline updating methods which often suggest a "standard check" at a predetermined number of years since the last update (10), which would be insufficient to be considered living.

Table 1: Key differences between traditional guidelines and living guidelines Cheyne et al. (forthcoming)

Key element	Traditional guideline	Living guideline
Guideline scope	Established at the start and does not change.	May be revised throughout the development process as required.
Prioritisation of clinical questions	Questions are prioritised for completion in the fixed period of the project.	Questions can be prioritised for varying intensities of living mode and priorities may be revised throughout the process, with opportunities to add new questions.
Engagement of clinical experts, consumers, stakeholders, leadership, and evidence team	For the fixed period of the project.	Ongoing. Needs a team culture that enables adaptive, dynamic, and responsive work
Evidence surveillance and searching	At a prespecified time point during development and typically not repeated before the publication of updated recommendations.	Continual and may be conducted at different frequencies for different recommendations (e.g., weekly, monthly)

1 * These are currently working definitions pending definitive approval.

Supportive information technologies	Information technologies can support conducting evidence reviews (e.g., screening, data extraction, GRADE assessment) and publication.	Technologies such as Covidence and MAGICapp have features that enable living guidelines.
Incorporating new evidence	Once, at the time of evidence review according to inclusion/ exclusion criteria.	Continual, according to decision thresholds for when to incorporate new evidence.
Effect estimates, summaries of evidence, evidence profiles and certainty of the evidence	Once, at the time of evidence review and recommendation development.	Continually updated and revised as new evidence is incorporated.
Approval and endorsement	Once, at the end of the guideline development.	At multiple time points, coordinated with external approval timelines and processes (e.g., from commissioning bodies). Approval for individual recommendations may be sought, rather than for the entire guideline.
Publication and dissemination	Once, after completion of guideline development.	Ongoing, at multiple time points, as new recommendations are generated, or changes are made to individual recommendations.

2.3 Principles underpinning a living guidelines model

The principles that underly the living evidence model and living guidelines are:

- Continual surveillance of the evidence
- Continual evidence synthesis, and recommendation development/updating
- Flexibility in timeframes and evidence synthesis approaches
- Robust evidence-based-practice methods including:
  - > Systematic reviews and Living Systematic Reviews
  - > Risk of Bias appraisal
  - > Use of GRADE (Grading of Recommendations, Assessment, Development and Evaluations)
  - > Evidence to Decision frameworks
- Rigorous guideline development which meets existing standards for evidence-based guideline development including:
  - > Strict and transparent management of conflicts of interest
  - > Consumer involvement in all stages
  - > Relevant stakeholder involvement
  - > Use of clinical and other expert panels
  - > Open publication and dissemination with external structured opportunity for feedback from health professionals, consumers and communities and peer-review processes

2.4 Evolving nature of Living Guidelines

Figure 1 illustrates the continual circle of a living evidence process to update evidence and recommendations. This is different to traditional guidelines which may remain static for years.

For living guidelines, the steps highlighted in **Figure 1** are not always sequential, as living evidence methods allow for an adaptive and iterative process. As mentioned in 2.2 and Table 1 - the frequency of evidence updates can be variable depending on needs, urgency and resources.

The Australia Living Evidence Collaboration considers:

- the "unit of update" is the individual living recommendation noting that some living guidelines may contain elements, including recommendations, that do not follow a living update process.
- different approaches may be applied to different living recommendations within the same guideline.
- the choice between applying specified evidence update processes across the entire guideline or tailoring methods for individual recommendations may be determined in a pragmatic approach considering feasibility, resources, and simplicity.

2.5 The interface between "rapid" and "living" guidelines

When differentiating between rapid and living guidelines, we make the distinction that a rapid guideline is one in which the speed of development of the baseline guideline is paramount; and a living guideline is one in which the process of development is iterative and ongoing, and the guideline (or recommendations within it) are continually updated. Thus, a guideline can be rapid, living, or both. More importantly, rapid guidelines are guidelines in which modifications are made to standards to enable the speedy production of guidance. In living guidelines, speed of production is important, but rigour is maintained. For more information on the differences between rapid and living please see Elliott & Jeppesen (11).

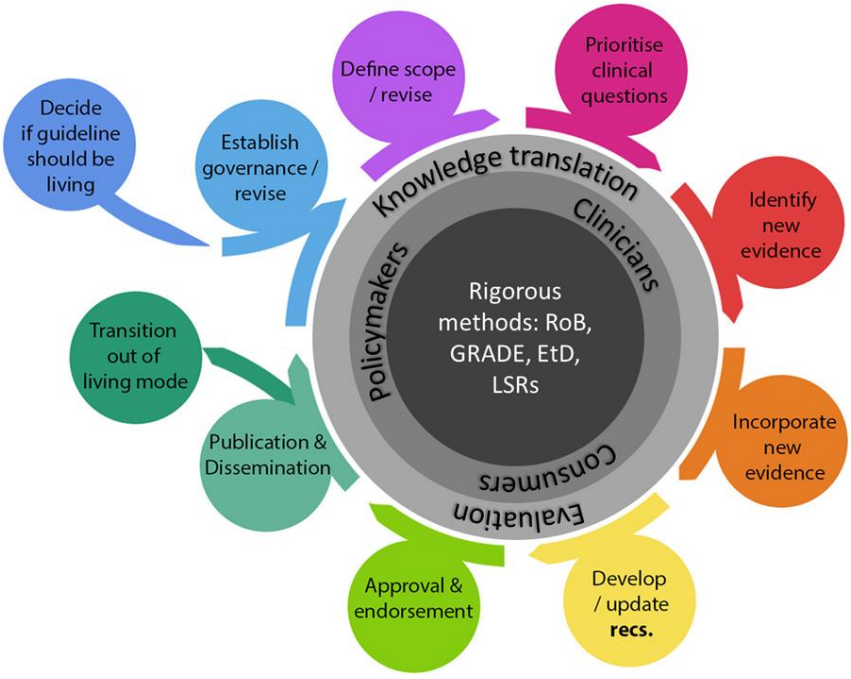

Figure 1: The 'spinning wheel" of living guidelines

3 When to consider a living guideline

3.1 Identifying when a living guideline is needed

While conceptually we could argue that all guidelines should be living and continually updated, not all health topics are changing at a pace that would justify a living methodology. In this section, we highlight criteria that may help guideline developers to decide when a living guideline approach is needed and most valuable. We also discuss two overarching approaches to developing living guidelines i.e. move an existing, traditional guideline into living mode; or create a living guideline from scratch.

3.2 Deciding to transition into living mode

Developers should start by ensuring that **all** the following criteria apply to the clinical area or topic in question. If only one or two of these apply, an alternative to a living approach may be more appropriate. The **three key criteria** are presented in **(Figure 2):**

1 Clinical question(s) is/are a high priority for decision-making, AND

2 There is uncertainty in the existing evidence AND

3 new evidence is emerging and/or expected to emerge.

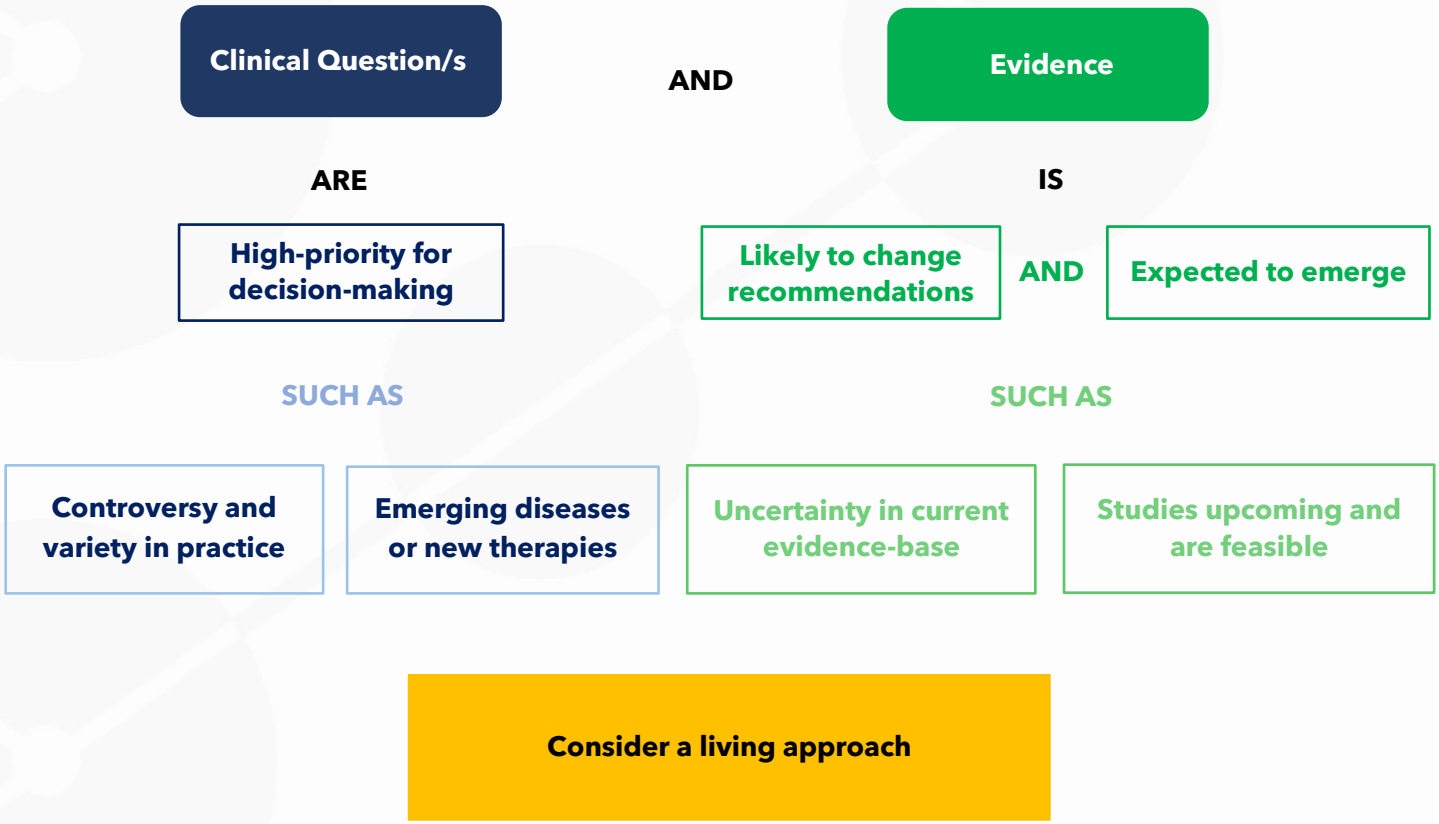

Figure 2: Living approach decision algorithm

3.2.1 The recommendations are a high priority for decision-making

Not all health topics are an equally high priority for decision-making. Examples of high-priority topics include:

- Areas of clinical controversy or "hot topics" for consumers or media (e.g. **ivermectin for treatment of COVID-19**).
- Clinical uncertainty about the best intervention or substantial practice variation. **(e.g. paediatric emergency management (12)).**
- The emergence of new diseases or changes in their epidemiological dynamics (e.g. **SARS-CoV-2, Zika virus** (13), **MPX** (14))
- The appearance of new syndromes, or adverse effects related to interventions that need urgent modifications to practice (e.g. **Paediatric Multisystem Inflammatory Syndrome** secondary to SARS-CoV-2 infection(15), adverse effects related to **pelvic mesh implants** (16))
- The appearance of a new class of therapies (e.g. **SGLT-2 inhibitors** for the treatment of type 2 diabetes, and its subsequent use for the treatment of heart failure (17) and management of chronic kidney disease (18)), new indications for already approved drugs, or in new populations.

3.2.2 New evidence is likely to change recommendations

As new, high-quality evidence emerges and timely recommendations are needed, a living guideline is valuable. Examples of this can be found in the response to the COVID-19 pandemic with treatments such as **remdesivir** (19) or **ivermectin** (20).

- **Existing evidence has reached high certainty**
  Some topics may be highly important for decision-making, however, there may already exist solid and robust evidence to underpin evidence-based recommendations and few remaining uncertainties surrounding that intervention or its use in specific populations, or it would require a very large, high-quality trial to change the existing recommendations.

  This might be the case if there are a large number of trials and meta-analysis shows a consistent direction of effect, there is high certainty of evidence, confidence intervals are tight and there is a large effect size for the intervention.

  Examples of these types of interventions are: **statins for cardiovascular prevention**(21), **folic acid supplementation in pregnancy**(22), or the efficacy of the **polio vaccine**(23)

If no new evidence is likely in the foreseeable future, then living guidelines approaches are unlikely to be a cost-effective or useful method.

3.2.3 New evidence is expected to emerge

Developers should consider a living guideline approach when there are signals that the topic in discussion is actively researched (ongoing trials, trial registries, in-vitro studies). Although some topics may be deemed a high priority for decision-making, new evidence may be unlikely in the foreseeable future for various reasons (e.g., ethical issues, difficulty in recruiting, special populations, lack of research funding, low prevalence…) Examples of these are rare diseases, exposure to likely carcinogenic risk factors, paediatric or pregnancy interventions, or the effectiveness of infection control procedures.

If new evidence is unlikely to change existing recommendations, then living guidelines approaches are unlikely to be useful.

3.3 Addressing feasibility

Feasibility is a key consideration for living guideline developers. Even if a topic or an area fulfils the three criteria above, it might be difficult to produce a living guideline without the appropriate skills, management, and resources. The feasibility of the process is very much context-dependent. Here we highlight the key considerations for guideline developers.

3.3.1 Funding

Initial stages

Having sufficient funding for the initial period that a guideline will be in living mode is critical. Living guidelines may be started first as a pilot program before evolving into fully-fledged living guidelines with longer-term support. The amount of funding required will depend on several factors including:

- Scope of the guideline (and how broad the topics selected are)
- Volume and complexity of evidence to be reviewed
- Establishment of governance structures
- Resources (human and financial) required to establish and maintain the governance processes and support the evidence professionals and guideline development team and guidelines operations
- Unpaid versus paid participation of healthcare professionals, consumers, panellists, experts, and consumers
- Access to software platforms and licensing costs
- Dissemination with media and communication support

Ongoing / maintenance

After a living guidelines program is established, future funding will be required for the maintenance of the program. Establishing commitment and support is important from the outset to ensure sustainability.

3.3.2 Governance structures for living mode

Guideline governance is a crucial component to guarantee that the flow of guideline production is maintained and sustained over time. There is no single or recommended structure for governance that is more suited to living mode but creating structures that are adaptable and not overly bureaucratic to enable swift changes and facilitate the approval and endorsement is essential for successful guideline development.
Having a clear and explicit structure and clarifying at what levels and by whom guideline decisions are made, and updated recommendations approved; will help streamline workflows, especially when new recommendations are urgently needed.

3.3.3 People and skills

Another key consideration to address in feasibility is whether multidisciplinary teams, with varied capacities and skills, are available. This is including the experts and guideline developers who are familiar with traditional guideline methods and able to adapt to the rapid pace of living guideline development. These capacities include having the appropriate evidence-based methodology and information management training, but also additional attributes regarding team attitudes and the ability to work in a fast-paced, rapidly changing environment and have a pragmatic approach to development processes.

In addition to the evidence team, guideline developers need to ensure they have the appropriate links with relevant professional and consumer organisations and peak bodies (such as professional colleges, and national NGOs) that may provide clinical expertise and consumer engagement.

Having an adequate pool of experts that understand the time commitments and rapid responses required for living guideline development is crucial, as both very large panels, as well as smaller ones, may have quorum issues, especially if this is a requirement for recommendation development and approval.

3.3.4 Time

Having a clear horizon for the expected frequency of updates, and time commitments required for panel meetings and guideline-developing activities is important to determine the resources required. The duration of involvement should be outlined in volunteer agreements, Terms of Reference and other governance documents. Equally important is to establish realistic expectations about guideline deliverables (not the right word) amongst all members of the guideline group.

3.4 Choosing the appropriate "mode" for living guidelines

Through this handbook, we highlight that there is no right or wrong mode of updating evidence and recommendations in a living guideline.

Not all living recommendations/guidelines need the same frequency of updates, and not all topics in the guideline necessarily have the same priority for updating. Choosing the right "mode" for updating each recommendation is crucial for sustainability and success.

For example, producing living recommendations at the peak of the COVID-19 pandemic when hundreds of new research publications were appearing every week required daily searches and weekly panel meetings to produce meaningful guidance and to process and incorporate all the newly available evidence. By contrast, for other areas with a slower or more stable evidence output, monthly or quarterly searches could be appropriate to address the new evidence.

There is a trade-off between updating very frequently, (which may consume important resources that could be used instead for longer-term maintenance work), versus not updating frequently enough, (which may decrease the trust in and relevance of the recommendations/guideline, or mean that the panels or the team lose momentum). Maintaining the right balance of engagement with stakeholders, and experts is vital for the living evidence process to be successful long-term.

An important feature and advantage of a living guideline is that the mode of development of a living guideline may also evolve. The frequency of updates for a given topic of question could be modified if the priority of the topic changes. Developers need to consider keeping a certain degree of freedom and adaptability to changing scenarios, to ensure that a living guideline is feasible in the long term.

By contrast, having overly complicated decision and approval structures will delay and slow down the guideline development process and frustrate the living process. For instance, seeking further rounds of comments among stakeholders, allowing additional parties to introduce modifications that need to go back again to panels, or having to fit the guideline publishing decisions to fixed meeting schedules from third parties.

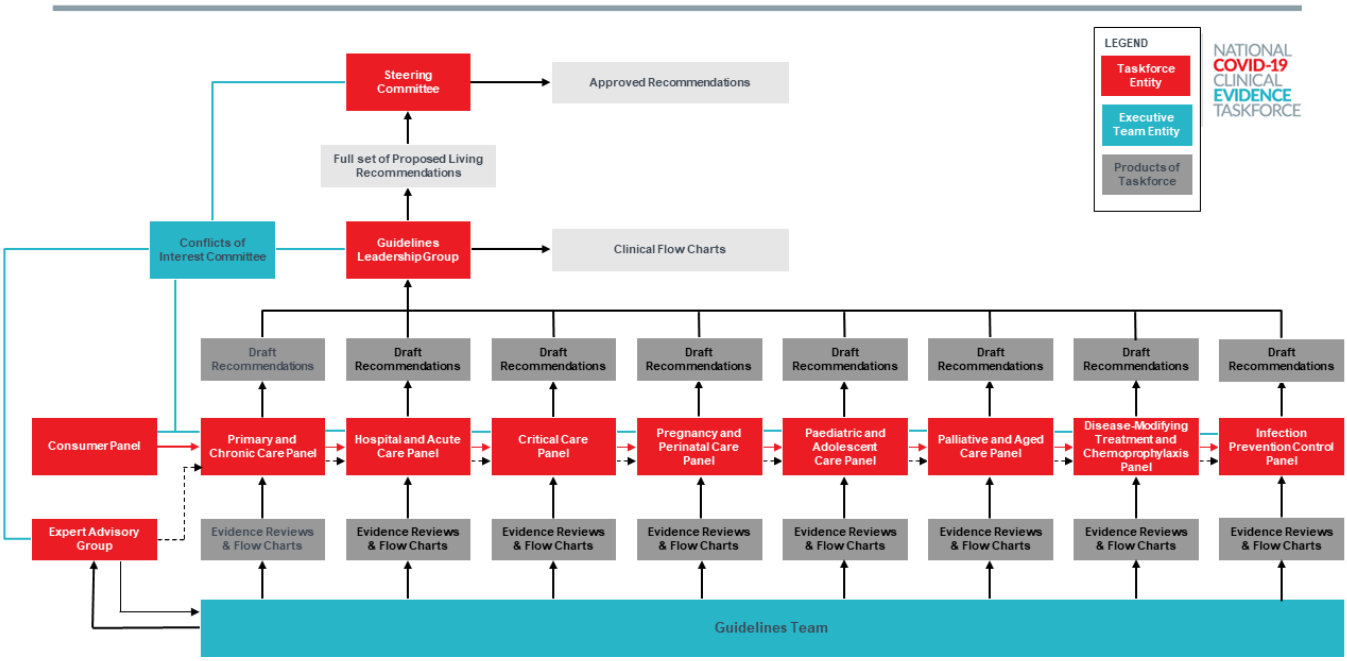

Figure 3: Example COVID-19 Taskforce Organisation structure and approval process

3.4.1 Upgrading structures for existing guidelines to transfer into living mode

For existing guidelines, it is important to address the need for updating the governance structure to support the living mode. It may require changing decision processes, especially regarding the development process, approvals, and endorsement of recommendations. Exploring new ways of communicating and gaining consensus on time is vital for swift approval and efficient functioning of a living structure.

3.4.2 Technology aids and introducing flexibility

Virtual meetings as opposed to in-person ones are a crucial enabler for living guidelines. This is particularly relevant where international organizations are involved, or across country-wide structures. Moreover, having the opportunity to discuss, and reach consensus offline or asynchronously (through email or other messaging platforms such as **Slack** or **WhatsApp**) can speed up decision processes between panel meetings. This may also introduce additional possibilities for the development process such as recommendation crafting (through **MAGICapp**), creating online surveys or polls, simultaneous editing of documents (**Google Docs** or **Office 365**) or further involvement in the triaging and appraisal of evidence (**Covidence**).

4 Question prioritisation

This chapter details how to identify, select and prioritise questions for a living approach. These approaches can be used for de novo living guidelines and when transitioning existing guidelines into the living mode, where the baseline recommendations and topics are already established, and it is a matter of maintaining the recommendations in living mode, more than creating recommendations from scratch. It is important to remember that parts of a living guideline may not be living, this is particularly true when transitioning existing guidelines into the living mode where the decision is to transition some but not all clinical questions and recommendations.

4.1 Identifying questions

Living guidelines and continual surveillance of the evidence provide an opportunity for the ongoing identification of new questions. For identifying new evidence in a certain clinical area, a broad search capturing all areas of the guideline scope should be created/developed. Any identified relevant studies can then be processed and assigned or triaged to a certain topic or clinical question, which can then be updated (or not) as deemed necessary. Living guidelines can identify clinical questions using the following innovative approaches:

- Evidence from initial searches, ongoing broad guideline searches, alerted to by stakeholders or the monitoring of clinical trial registries in areas of clinical uncertainty.
- Engagement with stakeholders, including guideline panels, healthcare consumers, and health professionals.
- Suggestions from the general public, via a website, communications team, or social media presence.
- Monitoring social media, mass media, and crowd-sourcing, for relevant topical issues.
- Contextual, political, regulatory, or other factors, such as new therapies seeking regulatory approval.
- Biological plausibility of treatment effect modifiers, such as information derived from in vitro data.

4.2 Selecting questions

Suitability for living mode can be assessed using the three key criteria for deciding if a guideline needs a living approach(24):

1. Is the question a high priority for clinical decision-making?
A question may be a high priority due to its importance to healthcare consumers and communities, stakeholders, clinical decision-making, public controversy, prevalence, the burden of illness, misinformation, patient safety, and political or other contextual issues.

2. New evidence is likely to change the recommendations?
This may be due to uncertainty in the existing evidence base, a lack of direct evidence, a high risk of bias in the available evidence, lack of evidence for specific sub-populations, equity issues, or changes to standard care and comparators, timing, route of administration or dosage of interventions.
A way to map uncertainty in existing recommendations is to consider which recommendations are consensus or conditional, where the underpinning evidence is indirect, where uncertainty remains for certain subpopulations (e.g. disadvantaged groups), the underlying studies are at high risk of bias, areas where guidance is non-existent but a high priority. This mapping will inform what recommendations are likely to be changed by new evidence.

3. Is new evidence expected to emerge?

This can be determined by searching trial registries or known trials can be tracked through regular engagement with professional societies, at annual scientific meetings or in partnership with trial networks within specialities. For existing recommendations, it is useful to map out the prior frequency that new evidence resulted in an update to the recommendations.

4.3 Prioritisation

The first step in prioritising questions for frequency of update of living mode is to rank questions according to both **importance to decision making** (ie How crucial is it to decision-making that any new evidence is rapidly incorporated into the recommendations?), and **timing:** of searching and updating recommendations (How rapidly moving is new evidence that is likely to change recommendations emerging?).

Assigning importance of questions

Questions need to be ranked/rated according to their determined importance so that resources can be directed towards the questions considered to be of higher importance. Rating priority systems can include referring to questions as fast, or slow streams (where "fast" streams include topics where it is more important that new evidence be rapidly incorporated), or low, medium and high, indicating their level of importance. The determination of importance will be guided by expert panels and consultation with stakeholders, including consumer groups.

Examples of processes that can be used for prioritisation / determining clinical importance to decision-making:

- Interview consumers, clinical experts, evidence team, and other stakeholders
- Conduct surveys, voting, nominal group techniques, Delphi approaches
- Hold stakeholder consensus meetings
- Rank clinical questions and recommendations.

Determining the timing of questions

Not only do questions need to be ranked for importance, but the timing of the updates (how regularly they are reviewed) also needs to be considered. Higher priority questions (e.g. those ranked/rated with higher importance, or from fast streams or high priority levels) will require more regular updates than questions with lower importance.) This will be impacted by several factors, including the ability to upscale the frequency of updating in the event of increased volumes of evidence, which inevitably relies on workforce capacity, streamlined processes, and funding.

Examples of processes that can be used to determine timing:

- Create an evidence map including the anticipated frequency, type, or size of the evidence base and what this means for timelines and future work planning.
- Determine the number and expertise of staff in the guideline development team, what is the funding, and for how long.
- Establish collaborations to share resource efforts across organisations.
- Respond to issues as they gain prominence in traditional and social media and/or within communities of practice.

5 Decisions surrounding living systematic review processes

Trustworthy guidelines must be informed by systematic reviews of the literature (25). In a guideline process, underpinning systematic reviews used to support the living recommendations also need to be living (26).

An early consideration in the living guideline development process is whether to 1) conduct a de novo living systematic review (LSR) for each guideline question, 2) update and maintain a previously published systematic review, or 3) use a hybrid approach that combines the two processes. This decision should consider the scope and type of question(s); the volume and frequency of new studies; whether systematic reviews (LSRs) already exist and if so, how often they are updated; and the developing organisation's infrastructure and available resources and expertise.

5.1 New LSR: "de novo" approach

A de novo LSR is conducted (evidence is systematically identified, appraised and synthesised) and maintained for each living clinical question in the guideline and includes "living" population, intervention, and comparator outcome (PICO) questions. LSRs incorporate relevant primary studies as they emerge. Guidance on the conduct of LSRs has been published previously (26).

5.2 LSR of published systematic reviews: "adopting" approach

In this approach, developers identify existing systematic reviews that address the clinical question(s), rather than seeking to identify and synthesise primary studies. This option is only viable if reliable, well-conducted systematic reviews are available, which can be assessed using tools such as AMSTAR-2 (27) or ROBIS (28). Ideally, an LSR should be used, if available, and the evidence summary updated in the guideline after each update of the LSR. Consulting with academic entities and foundations that produce SRs can facilitate this process. This includes the Cochrane Library and examples such as the Evidence-Based Practice Centres funded by the Agency for Healthcare Research and Quality in the US; and guideline-producing entities that commission systematic reviews, such as the World Health Organization and professional medical societies.

5.3 Hybrid LSR approach: combines the "de novo" and "adopting"

Developers may choose a combination of both approaches above within the same living guideline, for example by initiating a de novo LSR for some questions and relying on external LSRs for other questions. Another approach is to use an existing high-quality SR, either from an external source or produced by the team previously, as the basis of the evidence summary which the guideline development team can maintain in living mode, by incorporating emerging primary studies thereafter (Table 2).

Table 2: Strengths and limitations of evidence synthesis approaches

Approach	Strengths	Limitations
New living systematic review(s) covering "living" PICO questions.	Enables the guideline development team to control the speed of evidence incorporation and methodological rigour of the systematic review, including RoB assessments and synthesis; and to standardise approaches across questions within the guideline. New evidence can be incorporated according to the frequency of search and prioritisation decisions. It may be the only option available (no existing systematic review identified). Could be tailored either as a "rapid" or a" standard" systematic review.	Most resource-intensive approach. Risks duplicating efforts if other review groups or guideline developers are also conducting reviews answering the same clinical question.
Example	The National COVID-19 Clinical Evidence Taskforce (NC19CET) produced new living systematic reviews for each of the new disease-modifying treatments for the treatment of COVID-19(29–32)	
LSR of existing SRs and/or meta-analysis	Less resource-intensive and may enable Living guidelines, particularly for smaller teams. May decrease redundancy in research.	May decrease the frequency of updating. This may make the living guideline development process less reliable, as the team may not have a detailed knowledge of the primary studies. May introduce inconsistencies e.g. with other teams doing RoB assessments differently, using outcomes (or other parameters) that aren't in line with guideline developer needs. Reliant on identifying a review that exactly matches your inclusion criteria, or including only some studies, meaning steps such as meta-analysis may still need to be conducted by the team.
Example	Stroke guideline(33): For medical and surgical interventions only new large, randomised trials or individual patient data meta-analyses were considered for inclusion, due to the existence of systematic reviews on most topics.	

Hybrid approaches	Strengths	Limitations
New LSR for some questions, existing LSR/SR for others	Allows focusing of resources to conduct LSR on the high-priority questions where LSRs are most needed, or where there are no L/SRs identified for the question.	Different methods are used for different questions, which introduces complexity. Requires transparency about what methods have been applied for each guideline topic or question.
Updating existing SR/LSR with new studies	Provides a baseline that reduces resource efforts required to initially address questions.	Relies on the quality of the "baseline" review. May not fit completely the desired outcomes or review question(s).
Example	CARI Guidelines living guidelines on cholesterol lowering therapy in CKD(34) updated a published Cochrane review on HMG-CoA reductase inhibitors in people with CKD not requiring dialysis (35) for whom the absolute risk of cardiovascular events is similar to people who have existing coronary artery disease. This is an update of a review published in 2009, and includes evidence from 27 new studies (25,068 participants)	

5.4 Study screening and eligibility criteria

Eligibility criteria, often based on PICO components and study type, are traditionally fixed when a systematic review protocol is first developed, and this is generally considered a quality indicator of a review (27). In the case of guidelines, individual PICO questions are influenced directly by the overarching scope of the guideline itself. However, LSRs and living guidelines may opt for a dynamic set of eligibility criteria. While there are important methodological challenges to doing this in an unbiased manner, this flexibility enables the review to maintain relevance in an evolving context, such as with the emergence of new interventions. For guidance on how to develop eligibility criteria for systematic reviews see Henderson et al. (36). Below we will focus on the updating or adaptation of eligibility criteria over time and how to make relevant decisions.

Study selection is optimally performed by two independent reviewers. If only a single reviewer is predominantly available, having a second reviewer verify only the excluded citations or using automated approaches with natural language processing algorithms, may be useful (37) appraisal, and synthesis of all relevant studies for focused questions in a structured reproducible manner. High-quality SRs follow strict procedures and require significant resources and time. We investigated advanced text-mining approaches to reduce the burden associated with abstract screening in SRs and provide a high-level information summary. A text-mining SR supporting framework consisting of three self-defined semantics-based ranking metrics was proposed, including keyword relevance, indexed-term relevance and topic relevance. Keyword relevance is based on the user-defined keyword list used in the search strategy. Indexed-term relevance is derived from indexed vocabulary developed by domain experts used for indexing journal articles and books. Topic relevance is defined as the semantic similarity among retrieved abstracts in terms of topics generated by latent Dirichlet allocation, a Bayesian-based model for discovering topics. We tested the proposed framework using three published SRs addressing a variety of topics (Mass Media Interventions, Rectal Cancer and Influenza Vaccine.)

5.5 Evolving approach 1: Narrowing the eligibility criteria of an LSR over time

For a new clinical question or an area of high uncertainty, it may be that there is a paucity of high-quality data at the beginning of the LSR process. This may suggest a need for reasonably broad eligibility criteria. For example, early in the COVID-19 pandemic, there was a lack of robust randomised trial evidence for many clinical interventions, meaning that many systematic reviews opted to include case reports, case series or small cohort studies for evidence of benefits or possible harms. Over time, as other study types were published, eligibility criteria could be refined to exclude lower-certainty study designs, such as nonrandomised studies, in favour of more reliable data.

5.6 Evolving approach 2: Broadening the eligibility criteria of an LSR over time

An alternative approach could be to start with narrow eligibility criteria for study design and then broaden them over time. This would be appropriate for questions where high certainty of evidence is initially sought, but searches and literature monitoring do not yield sufficient evidence to inform recommendation development.

These responsive modification approaches apply to other elements of the eligibility criteria. Modifying the target population (to increase or decrease its scope), modifying the interventions (or comparators) to be included (e.g., as new treatments emerge), as well as other elements of the eligibility criteria may be appropriate as the knowledge of the disease area evolves (Table 3).

Table 3: Strengths and limitations of evolving approaches for eligibility criteria

Approach	Strengths	Limitations
Evolving approach 1: Broad to narrow	• More efficient use of resources. • As evidence accumulates, the scope of the protocol can be narrowed to include only a priori high-quality studies. • Allows identifying subgroups that may benefit (or not) from intervention	• It may create confusion if methods are not transparently reported. Initial evidence may be "insufficient" to inform recommendations hence potentially creating unnecessary reviewing. • May decrease the number of eligible studies. This may decrease the generalizability of recommendations.
Example(s)	The Infectious Disease Society of America (IDSA) COVID-19 diagnosis guidelines(38) developed in collaboration with USGN, started by including all studies regardless of peer review but the pre-prints became a huge drain on resources. In later updates, we decided to only include published papers as there was more evidence at that point. Similarly, more strict decisions were applied about acceptable reference standards as the guidelines were updated, and more evidence became available. NICE COVID-19 Guideline(39): initially used one broad search to cover all recommendations within the guidelines, but these have tightened over time. This was mainly because some of the initial eligibility criteria (like considering evidence from the Middle East Respiratory Syndrome (MERS) virus) were no longer relevant. Eligibility criteria around study types also narrowed over time, as initial searching was much more inclusive in the early phase.	

Approach	Strengths	Limitations
Evolving approach 2: Narrow to broad	The initial approach is narrower and less resource intensive. Recommendations might be more generic and less specific. Can help identify "indirect" evidence to inform recommendations where little evidence available. In the context of rapid, living guidelines, additional sources of information may be considered such as trial registries and regulatory approval data (obtained in confidence).	May be perceived by guideline users as "lowering standards". Requires careful documentation and transparency of changing eligibility criteria over time. Requires careful consideration when extrapolating from populations, comparators, or dissimilar outcomes. Broader eligibility criteria may affect GRADE ratings and Evidence to Decision (EtD).
Example(s)	Stroke guidelines(33) increased their population scope to include all cardiovascular disease patients when reviewing the concordance of medication. In the IDSA COVID-19 antigen testing diagnosis guidelines(40), we had to broaden our PICO when discussing diagnosis for patients who were immunocompromised because of feedback that required we address different types of immunocompromised based on the type of immunosuppression they received.	

5.7 Use of pre-prints, preliminary data, and regulatory data.

The development of pre-print platforms (such as arxiV, medRxiV, Research Square... etc) has meant an important expansion of non-peer-reviewed scientific literature (41). The preprint phenomenon poses special challenges for living evidence synthesis and for the development of appraisal tools and methods that consider issues specific to preprint articles. Reviewers may opt to exclude preprints altogether on the basis that awaiting peer review may help ensure that only reliable evidence is included.

However, there have been instances of important, practice-changing, high-quality trials being made available as preprints to accelerate their translation into guidelines and clinical practice (42,43) controlled, open-label, adaptive, platform trial comparing a range of possible treatments with usual care in patients hospitalized with COVID-19. We reported the preliminary results for the comparison of dexamethasone 6 mg given once daily for up to ten days vs. usual care alone. The primary outcome was 28-day mortality.\nResults 2104 patients randomly allocated to receive dexamethasone were compared with 4321 patients concurrently allocated to usual care. Overall, 454 (21.6%. As such, LIVING GUIDELINE developers may opt to consider certain preprints to be eligible. We advise that guideline developers implement appropriate literature surveillance measures to identify if articles are published in peer-reviewed journals and document a priori how preprints are monitored. If preprints are used to inform recommendations, then this should be stated, and the data rechecked and incorporated once the peer-reviewed data is published.

6 Search methods for living guidelines

For additional information please see McDonald et al. (forthcoming)

6.1 Preliminary overview of the evidence in an area or topic

When conducting a living guideline, or deciding if a living guideline approach is required, it is strongly recommended to "map" the available evidence before starting, especially if the living guideline is developed de novo, or the topic that the guideline covers has emerged recently. Preliminary searches as well as contacting experts may help facilitate identifying the uncertainties surrounding the topic, the gaps in current guidance, as well as the expected volume of evidence appraisal that will be required. Having an information specialist to inform preliminary searches and overall search strategies is strongly encouraged.

The decisions about this initial scoping search process are pragmatic and do not preclude any shortcuts into the development methods later (doing a proper systematic search for the selected questions of the guideline). The aim of this initial search instead is to provide clarity on question prioritisation as highlighted in Chapter 4 and to guide decisions regarding living mode including:

- Is the guideline suitable for living mode? (See previous criteria in **Chapter 3**)
- What is the amount of work required? What are the team capacity and skills required to appraise the evidence?
- What are the gaps and areas in need of guidance?

6.2 Identifying previous guidance and related content

A good place to start preliminary searches is to identify guidance (either living or traditional) from other reputable national or international organisations. A common problem when attempting to identify previous guidelines is that not all of them are indexed in biomedical databases. A few reputed organisations may provide examples of guidance developed in an area or topic. A non-exhaustive list of resources to check includes:

- Internationally recognised organisations and guideline repositories: WHO, GIN, NICE, NHMRC, SIGN
- PubMed (with a guideline search filter)
- Reputable professional and scientific societies
- Grey literature, pre-print servers, media and social media

Besides scoping out existing guidance and research, developers may want to identify potentially unpublished emerging evidence. Accessing clinical trial registries such as clinicaltrials.gov or the EU Trial registry may help identify trials appearing soon.

6.2.1 Identifying previous systematic reviews and scoping reviews

The next step is to identify Systematic Reviews of the literature or to conduct a full scoping review of the area or topic to develop guidance. For further guidance on how to conduct a scoping review please see Munn et al. (44).

6.3 Search Methods for a new living guideline

The search processes for living guidelines and addressing specific PICO questions do not differ substantially from traditional guidelines. However, there may be a few pragmatic decisions to speed up the process and streamline the outputs. Once the inclusion and exclusion criteria are defined for the specific PICO questions and depending on the scope of the question to answer, pragmatic decisions about the search strategy may need to be considered, especially between a highly specific search strategy versus a broader all-encompassing search approach. Factors to consider include:

- Searching in only one or more than one database (e.g. PubMed) to include only very high-impact publications and trials) compared to a multiple database search for instance, for non-pharmacological interventions.
- Limiting searches to one database (e.g. PubMed) versus multi-database searches
- Limiting searches to specific types of evidence, such as systematic reviews versus primary studies, or randomised trials versus observational studies.
- Searching for systematic reviews and meta-analysis versus searching for primary evidence.

Researchers may consider a broad, multi-database search strategy to begin with, but conclude that there is little impact or added benefit of screening supplementary databases. By contrast, searching may include instead pre-print servers, where in the case of an emergency or where rapid appraisal of the evidence is needed (e.g. during the COVID-19 pandemic) this may expedite the reviewing process since the results appear until the recommendations are published.

We identify two main models for searching in living guidelines:

- A single "broad" overarching search that captures all the emerging evidence in an area or topic
- Highly targeted PICO question-specific multiple searches

6.3.1 Single overarching search

High sensitivity with a broad focus

With this approach, the search strategy is aimed at capturing "all" relevant literature for a whole area or topic (e.g. management of stroke, treatments for COVID-19). Traditional filters for study type can still be used (e.g. only RCTs) and pragmatic decisions can be also made (single database search, include or exclude pre-print servers). Using this approach has advantages and disadvantages that the developing team needs to consider:

- A single search for a broad topic means "any" relevant study is more likely to be included, for instance for areas with high uncertainty, complex interventions, with multiple treatment options.
- The single search approach still requires a rigorous screening process of the results and triage into specific categories. If a guideline is composed of multiple working groups, a first round of study "triage" that assigns the search results to specific subgroups might be needed.
- This strategy may be more suited for existing guidelines where there is a "baseline" knowledge base, and the aim is to transition to living mode and "update" with new evidence as it becomes available. An example of a living guideline that uses this type of overarching search is the Australian Clinical Guidelines for Stroke Management (33)(45).

6.3.2 Highly specific searches

High specificity with a narrow focus

This approach is similar to the search strategies that may be used for systematic reviews and traditional guideline development. When developing de novo guidelines where specific questions or topic areas are only in living mode, this approach may optimize resources and reduce unnecessary screening. For instance, in our living Diabetes guidelines(46) and Musculoskeletal guidelines(47) where some specific treatments or therapies are selected for living mode, as opposed to areas where multiple treatments or interventions are considered. The trade-off to consider with highly targeted searches is the chance to miss additional developments or topics that may be deemed appropriate for inclusion in the guideline and are not currently considered. For further clarification on search strategies please see McDonald et al. (forthcoming).

6.4 Ongoing evidence surveillance

How frequently the search is updated in a living guideline, will be influenced by the evidence pipeline (including evidence synthesis, recommendation development, panel meetings and publication). There is no established "consensus" on how often the search strategy needs to be performed and updated for a guideline to be considered living but as a guide, **searches for living guidelines, or specific topics or questions should be conducted at least every 3 months.**

For certain research questions and topic areas more frequent (e.g. daily or weekly), search updates are needed. Topic areas, with moderate uncertainty or without an important amount of research output, may consider longer timeframes. However, the continual process of evidence development requires a continual input of "research" to be maintained into living mode. If a certain frequent search update cannot be maintained or is not needed, decisions surrounding the suitability of living mode need to be reconsidered.

6.5 Reporting search results

Living guidelines may differ from traditional guidelines and systematic reviews in how the search is reported, to reflect changes over time in sources, frequency and search strategies. However, as with traditional guidelines and reviews, it is important to report the search methods transparently, documenting changes in the approach as the living guideline evolves. When using software platforms (such as MAGIC) or specific guideline websites and social media, a suggested good communication practice is to keep a regular update of the search results as an "evidence tracker", where the studies that are detected, reviewed, or about to be included are reported clearly. If there are further refinements or modifications to the question and therefore to the search strategy, it is important to communicate any changes in the search as well as identify clearly in which version or update of the guideline it was changed.

6.6 Assessing and refining search methods

An important aspect of "living searches" is the continual evolution of the area of research that in many cases would require changes and refinements to the search strategy. In situations for instance, of emerging diseases, search strategies may need to use different synonyms as well as collections of terms to capture all the relevant literature of an emerging topic (for instance, on the management of post-acute COVID-19, also coined "long covid"). This may motivate changes over time as the disease or area becomes more established, and for instance, MESH terms are created. Modifications to the inclusion and exclusion criteria and changes to the search strategy (e.g., inclusion of observational studies or randomised controlled trials only as the evidence for a certain topic evolves and decisions on whether to use a certain type of evidence may be pointed to be inadequate afterwards.)

7 Evidence appraisal and synthesis

For additional information please see Fraile Navarro et al. (forthcoming)

7.1 Evidence synthesis

Compared with traditional guidelines, developing evidence profiles for living guidelines presents unique challenges largely due to the higher frequency of updating.

New evidence will lead to changes in effect estimates and levels of certainty in GRADE (Grading of Recommendations, Assessment, Development and Evaluations), particularly in the GRADE domains of imprecision and inconsistency (48). Deciding when to update the existing evidence base with new evidence requires careful consideration. For meta-analysis, key statistical considerations for LSRs are referred to in a paper by Simmonds and colleagues(49), provided reviewers are aware that results may change at later updates. If the review is used in a decision-making context, more caution may be needed. When using standard meta-analysis methods, the chance of incorrectly concluding that any updated meta-analysis is statistically significant when there is no effect (the type I error.

The Evidence to Decision (EtD) framework will also become living and benefit versus harms profiles may change as the evidence evolves, or changes in the health system impact other aspects of the recommendations such as feasibility issues due to access to equipment, training or approval of treatments.

Assessment and synthesis of the evidence are supported by using information technology programs, such as MagicApp and Covidence (50)(51). MAGIC is an online platform that allows the publication of guidelines, including evidence profiles, evidence summaries and recommendations. ALEC has worked with MAGIC to include features specifically designed for conducting living systematic reviews and guidelines. These include tagging new or updated recommendations, the ability to update evidence profiles, track changes and version history. These features have made ALEC living guidelines easier to maintain.

7.2 Evidence appraisal

Developing living evidence profiles presents unique challenges largely due to the higher frequency of updating. Deciding when to update the existing evidence base with new evidence requires careful consideration.

New evidence may lead to changes in effect estimates and levels of certainty in GRADE (48). Assessment and synthesis of the evidence base can be accelerated by software and online platforms such as Covidence (51), Distiller SR (52), Rayyan (53) or EPPIReviewer (54) for study selection and data extraction and GRADEPro GDT (55) or Making Grade the Irresistible Choice (MAGICapp) (50) for evidence assessment certainty rating and recommendation development.

7.3 Data extraction

Data extraction follows well-established methods, as per Cochrane's methods for SRs (36) and LSRs (26). Although using two reviewers across the evidence appraisal and extraction process is considered best practice, often resource and time considerations require simplified approaches (Table 4).

Table 4: Approaches for evidence appraisal

Approach	Specific to Living guidelines	Considerations
Individual versus duplicate data extraction (e.g. second reviewer looking at exclusions (56,57)	No	Pre-calibration with a sample of studies and establishing mechanisms of disagreement-solving are required.
Use of pre-customised data extraction templates.	No	Can be calibrated throughout the initial development, as the first few studies emerge.
Evolving data extraction forms	Yes	If the guideline requires it, data extraction templates may evolve and adapt as clinical questions evolve.
Example(s)	(External example) In the IDSA COVID-19 diagnosis guidelines(40), our data abstraction evolved to assess new subgroups. (e.g., vaccinated versus not vaccinated and emerging variants.)	
Use of SR software platforms	No, but there are opportunities for specific functions for LSRs and living guidelines in the future.	Eases calibration process. Facilitates data extraction and allows exporting and sharing of data. Helps to organise review questions and add new studies over time
Example(s)	(External example) In the IDSA COVID-19 guidelines(58), Excel was used for some questions and Covidence for others.	
Data sharing among different developing teams	Yes	If an external LSR is also being conducted, cross-checking data extractions from other groups could be used in place of second data extraction.
Example(s)	NC19CET(29) and NICE(39) have collaborated by sharing data extraction sheets and evidence profiles evaluating treatments for COVID-19.	

7.4 Risk of bias assessments

Risk of bias (RoB) assessments are a critical step in guideline development and should not be missed or substantially modified when developing living guidelines. Preconfigured RoB templates and specific software can speed up the process. Reviewers need to be properly trained in these assessments before execution, calibration and resolving disagreements, as this is a crucial phase in living guidelines.

7.5 Modified approaches to appraisal

Usually, a single-reviewer appraisal of RoB is not recommended given that such appraisal requires making judgments. Where a living guideline is developed rapidly, with limited resources and a high level of methodological expertise within the guideline development team, this may be a potential consideration for developers. For instance, using sample checking (e.g. 20% or after reaching a sufficient agreement between reviewers) by a second reviewer. Another possible solution is a collaboration between different teams, especially in situations where multiple national guidelines need to be produced as rapidly as possible (e.g. international public health emergencies). We encourage guideline development teams to consider collaborative approaches and establish mechanisms for sharing RoB assessments through the use of online platforms or review tools (50,51,53,55). Where included trials have been appraised in existing reviews, using these appraisals in place of an additional reviewer can also decrease resource requirements.

If guideline developers use a published SR-based approach (See **Section 5.2**). or a hybrid approach (See **Section 5.3**), a detailed examination of the existing review's RoB appraisal should be considered, especially if the review has been developed by external reviewers.

7.6 Other considerations: Use of pre-prints, preliminary data, and regulatory data.

Standard evidence appraisal processes do not currently take into consideration the potential for erroneous or falsified data to be present. This consideration has been a problem in the past both with pre-prints and published studies (59). However, while a published study can be retracted, there is no clear process to retract pre-prints - they may never be removed or taken down, nor published. Approaches for monitoring pre-print status as well as setting deadlines for publication (especially for controversial or unproven treatments) should be considered by developers (Box 1).

Box 1: Examples of pre-prints and preliminary data from NC19CET

1. On occasion and with the approval of the Sponsor, the Australian Therapeutic Goods Administration has provided NC19CET(29) with confidential Clinical Study Report (CSR) data for trials specific to COVID-19 treatments. These data are significantly more comprehensive than those provided in a peer-reviewed or pre-print publication and subsequently require more in-depth analyses. Although this process is more resource-intensive, the provision of a comprehensive study protocol and individual patient data facilitates more robust data analyses and RoB assessment.
   This process does pose other challenges, however, particularly around ensuring that data supporting recommendations can be made publicly available within EtD and Summary of Findings tables.

2. NC19CET(29) established a pre-print policy that evolved through the pandemic. First, it established that pre-print authors were to be emailed after 2 months if the study was not published in that period. A revised version later removed this step as only very small studies have not reported pre-print results and authors who were contacted did not reply to enquiries, therefore considering it an inefficient approach. This policy also established that pre-print studies that raise concerns (such as unproven treatments e.g. ivermectin) needed to be reported in the evidence summaries.

Similarly, in certain situations, trial data may be reported to clinical trial registries before publication, or guideline developers may be given access to confidential trial data submitted to regulatory agencies or given academic access in confidence. It is important to consider how this information is addressed and presented to the panel. Special considerations need to be given to conducting the appraisal process and RoB assessments (Box 1).

7.7 Evidence synthesis approaches for Living Guidelines

Core methods for assessment and synthesis of the evidence are the same as those of traditional guideline development but may be modified to facilitate a more rapid approach and to allow continual incorporation of evidence while maintaining methodological rigour.

7.7.1 Dynamic changes to evidence summary

The key feature of living guidelines is that the certainty and direction of the evidence underpinning the recommendations may be modified more frequently than in a traditional guideline. One possible result of moving from a low to high certainty of evidence is that this may facilitate a change in the overall strength of a recommendation, for example, moving from a weak to a strong recommendation (60). Aims and Objectives It is generally believed that evidence from low quality of evidence generate inaccurate estimates about treatment effects more often than evidence from high certainty. In addition, as a living guideline evolves the evidence base for some questions can become more certain and guideline teams may choose to change the frequency of future updates. As the living guideline process commences, new questions will arise, often with very low or low certainty evidence. The arrival of new treatments can result in changes to strong recommendations, and new research on disease mechanisms can also mean a change to long-standing recommendations.

7.7.2 Updating meta-analysis

Previously, concerns have been raised that updating meta-analyses can lead to an increase in type I error (rejecting the null hypothesis while true) rates (61) and therefore, an increased risk of chance findings. There are different views on whether adjustment for type I error inflation is required in a frequently updated meta-analysis (49,62){"id":"BPeyvGfv/l6Xvc0wK","uris":["http://zotero.org/users/local/gzolYSAH/items/AJJ6UR9B"],"itemData":{"id":"tK5dLGD9/z8pe9iWm","type":"article-journal","abstract":"A living systematic review (LSR but currently, the Cochrane Scientific Committee does not recommend adjusting when updating meta-analyses (62). A full discussion is beyond the scope of this paper. Developers are encouraged to consult statistical experts when preparing for conducting this type of analysis in living guidelines.

8 Developing and updating recommendations

8.1 De novo recommendations

The initial development process of a recommendation does not vary from a traditional guideline approach. However, in the context of living guidelines, developers need to bear in mind that the frequency of updates may point to further iterations and refinements of a given recommendation affecting the recommendation creation process.

8.2 Updating existing recommendations

Living guideline approaches to the assessment of the certainty of evidence and strength of recommendations fit neatly within the standard GRADE approach. In the GRADE approach the certainty of evidence and how it translates into the direction and strength of recommendations are not considered to be a "static" attribute for a given clinical question, but rather based on a comprehensive review of all the available evidence at a particular point in time; potentially revised in a future guideline update.

8.3 Update frequency of recommendations

A fundamental principle of living guidelines is that recommendations are updated in response to new, potentially important evidence. Developers may initially be tempted to update living recommendations frequently, or when there are only minor changes in the underlying evidence base. However, this approach can be highly resource-intensive without concomitant improvements in the quality and usefulness of recommendations.

There is a trade-off to consider between updating too frequently (which may consume important resources that could be used elsewhere) and not updating frequently enough (which may decrease the relevance and utility of the guideline, contribute to loss of momentum, and ultimately decrease the value of a living approach).

Maintaining the right balance of engagement with stakeholders and experts is vital for a living guideline to be maintained long-term. For instance, producing guidelines at the peak of the COVID-19 pandemic required daily searches and weekly panel meetings to process and incorporate all the newly available evidence and produce a meaningful, relevant and current living guideline. However, for other areas with a slower evidence output and/or a greater degree of clinical certainty, monthly or quarterly searches could be sufficient to identify and appraise the new evidence (Box 2).

Box 2: Examples of recommendation update frequency:

For the COVID-19 living guidelines (63), searches were initially run daily across all topics and PICO questions. Later as the rate of new research evidence slowed, a priority system was introduced, so only high-priority searches were conducted daily, and others moved to a weekly basis.

In the Stroke living guidelines(33) searches were set up to run monthly. Later, while the search and review were still monthly, the process changed from involving panels every 2-3 months to every 6 months unless a critical new study is identified.

While any specific cut-off on update searches is arbitrary, a living guideline that does not have updated searches and reviewed new evidence after more than 6 months is unlikely to be accepted to be undertaking a living approach. If the topic(s) or area of interest of the guideline is not particularly evolving, developers may consider transitioning the guideline (or parts of it) into a more traditional updating cycle.

8.4 When to incorporate new evidence? Triggers for synthesis, appraisal, and incorporation into recommendations

While guideline developers and stakeholders may ideally want to include new evidence as soon as it emerges, resource considerations, and judgements surrounding guideline priorities (Cheyne et al. (forthcoming)), can prompt decisions to incorporate it more selectively. Decisions surrounding incorporation will depend on eligibility criteria, but also the likely impact of a newly identified study on existing recommendations (in which case the decision is made after an initial appraisal); additional considerations may also prompt developers to delay or prioritise evidence incorporation and recommendation creation or update. To minimise the opportunity for bias, decisions about criteria and thresholds for inclusion need to be pre-specified. In this section, we highlight approaches and considerations that modify the selected approach.

8.4.1 Immediate incorporation: as soon as evidence emerges

In the default approach, as soon as a new study is identified the whole evidence synthesis process and recommendation update are undertaken. It allows for the fastest incorporation and enables developers to always have the latest evidence available in the recommendations. It could be suitable for very high-priority areas with lots of uncertainty. However, it is resource-intensive and may create an unnecessary workload if full evidence review incorporation is undertaken with little or no impact on recommendations.

8.4.2 Trigger-based incorporation: prompted by predefined factors

In this approach, a set of predefined triggers is used for deciding when to incorporate new evidence into recommendations (Table 5). These approaches require that guideline developers, panellists and stakeholders agree to the given strategy beforehand, to avoid introducing bias in the selection process (e.g. establishing minimally important differences, or a specific event or sample size). If studies do fit the eligibility criteria for a given clinical question but do not merit triggering incorporation, their identification and decisions surrounding it should be reported transparently. The use of a trigger-based system may create a backlog of studies to appraise and incorporate. Once a backlog is created, a clear timeline for incorporation and monitoring should be agreed upon and implemented.

8.5 Evidence to Decision (EtD)

Similarly, the Evidence to Decision (EtD) framework also becomes living and could equally prompt modifications in recommendations after the factors in the framework are considered and modified. Given the evolving nature of living recommendations, and the potential for their development in certain situations, a suggested approach for EtD framework development for rapid recommendations with an initial paucity of data, is to consider incorporating certain elements at different stages after the initial recommendation. Equally, the update of a recommendation may not only be triggered by a change in the evidence but also due to changes in non-effectiveness components of the EtD (e.g., a change in the cost of therapy). Examples of modifications to elements of the EtD framework (64) in living guidelines can be seen in Table 6.

Table 5: Trigger-based incorporation approaches

Approach	Considerations
"Trigger-based" incorporation approaches	Guideline developers, panellists and stakeholders must agree to the given strategy beforehand, to avoid introducing bias in the selection process. (e.g. establishing minimally important differences, or a specific event or sample size). If studies fit the eligibility criteria considered for a given clinical question but do not merit triggering incorporation, their identification and decisions surrounding it should be reported transparently. The decision of not to trigger an update and "waiting" will create a "backlog" of studies to be incorporated in future updates, based on the pre-set priority for a given clinical question.
Types of trigger-based approaches	
Size-based (participants or number of events)	New studies are incorporated when a critical N is reached for single or multiple studies (e.g. including studies only above n=100 and/or including studies when subjects are included in metanalysis = 100).
Precision-based	Studies are incorporated into recommendations when we anticipate that the addition of new studies would improve the precision of the current meta-analytic estimate. Thus, if the confidence interval of the new estimate changes in relation to a decisional threshold, a rationale for incorporating the new studies becomes more compelling. A special case of this trigger is when the decisional threshold is null, in that case, the criteria for including studies becomes significance based.
Certainty-of-evidence:	When using GRADE(48) for evaluating the certainty of evidence for a given outcome, new evidence is incorporated, and recommendations are updated only when there is a change in the certainty of evidence or direction of effect that may merit a change in a given recommendation (e.g., a new study would modify the certainty of evidence of a benefit on overall mortality from low to moderate). It is plausible that guideline developers chose null as their threshold for certainty (e.g. they would update the recommendations if the results became statistically significant).
Minimally important clinical difference(s):	The panel may agree beforehand that a given magnitude of effect in a certain outcome is required for changing a recommendation (e.g. difference is 20 fewer per 1000 events for mortality). The update is only triggered when a given effect size is reached (potentially in combination with significance-based and certainty-of-evidence based approaches).
Other considerations	Opinions of clinical experts (panel or non-panel members) may be important when new studies could potentially change overall effects and modify clinical practice. Also, it is important to consider if a recent, well-known trial is not included, it may impact the guideline's credibility and decrease its impact. Clinical experts may also identify if major new studies are imminent, and it is recommended to delay incorporating other but probably less important new studies.

Table 6: Evidence to Decision considerations

EtD - item	Asynchronous	Considerations & Example(s)
Benefits and harms	No	In vitro or post-commercialization studies may also inform harms.
Certainty of the evidence	No	May reflect the certainty of the main outcome (e.g. mortality) or all important outcomes.
Preferences and values	Yes	For instance, a drug is recommended, and then later a consumer panel reviews the recommendation, and their input is considered. Also, new studies on P&V may emerge and be compiled later. Please see Synnot et al. (forthcoming).
Resources	Yes	A drug may reduce its cost (e.g. patent is ending). Or a new cost analysis may be published that modifies its cost profile.
Equity	Yes	Sometimes an intervention may increase inequity, but changes to the broader health system modify it (e.g. increasing access in rural and remote areas)
Acceptability	Yes	Interventions may be deemed less acceptable, but changes in preferences or the risk profile may deem them more acceptable.
Feasibility	Yes	Feasibility of an intervention modified in relation to all previous factors, and broader health system considerations.

8.6 Conflicts of Interest management

Clear and transparent reporting of conflicts of interest (COI) remains a key element of living guidelines as in traditional guidelines. However, given the dynamic nature of the guideline and the recommendations as well as of the COI themselves, it would require at a minimum, constant and periodic updates to the COI declaration, which may as well reflect dynamically on the development of the recommendations. What is/are the most appropriate approach(es) to manage COI in living guidelines is still an area in development.
One approach to consider is the use of specific tools to assess dynamically COI. An example of this can be found in the MSK Guidelines which have developed specific tools to re-evaluate and consider COI in the process of a living guideline using a dynamic COI matrix that is periodically re-assessed and provides a score for each participant. For more information please see here and here.

9 Consumer engagement

9.1 What we mean by consumer engagement

Living guidelines follow established guideline methods, (24) Cheyne et.al(forthcoming) meaning they include the perspectives of patients, people with lived experience, carers, the public or their representatives ('consumers') (9)(65). Consumers might join the steering group, guideline development group (GDG), or consumer advisory group, or take part in workshops, focus groups or interviews at one or more stages of the process. (66,67) Commonly, consumers contribute to a guideline as one of a few consumer members of the GDG (66). These activities constitute 'consumer engagement', i.e. the active involvement of consumers in dialogue with guideline developers, resulting in informed decision-making at any stage of the process (adapted from Concannon et al (68)).

This guidance draws upon the experiences of guideline developers and consumers involved in four ALEC guidelines (stroke, COVID-19, diabetes, and inflammatory arthritis)(45)(46)(29)(47) and in the UK's National Institute for Health and Care Excellence (NICE) guideline on COVID-19 (39).

Below, we highlight several considerations regarding consumer engagement that we found to be unique to living guidelines. Guideline developers may wish to think carefully about how they might incorporate or address the considerations. We are not prescriptive about specific methods or approaches that guideline developers should use as many other factors will determine how consumers are engaged in an individual guideline, such as the guideline topic, the guideline stages in which consumer input is needed, the backgrounds, experiences and preferences of the consumers and guideline developers involved, along with resource considerations. Instead, we present a detailed description of how consumers are engaged in our five living guidelines.

9.2 Considerations regarding consumer engagement in living guidelines

9.2.1 Build on established best practices in consumer engagement

There is considerable research and guidance available for guideline developers about how to engage consumers in guidelines in ways that are meaningful and beneficial for all parties (69) (1) (70). For example, co-developing the engagement approach with consumers, having a careful and planned recruitment strategy, establishing clear expectations, providing a comprehensive orientation and ongoing technical and other support, having a welcoming and inclusive environment, and engaging skilled and experienced meeting facilitators, are all established features of 'good' consumer engagement.

The experiences of consumers and guideline developers involved in the ALEC and NICE living guidelines highlighted that the fundamentals of good practice still apply to a living approach. For example, consumers in some of our living guidelines recommended induction and training could've been more comprehensive or practical, and highlighted greater efforts could be made to reduce the use of technical language and jargon. Conversely, consumers praised the critical role of the meeting chair in supporting their active involvement and that they felt welcomed, valued and respected.

Given the novelty of living guidelines and the complexity of transitioning to a living guidelines model, guideline developers should be experienced in working with consumers and, ideally, operate within an organisation with in-house expertise. Guideline developers must build upon a solid base when it comes to consumer engagement and be able to plan and support best practices throughout the endeavour.

9.2.2 View the consumer engagement as 'living'

We found it necessary and helpful to view the approach to consumer engagement as 'living'. In this way, all stakeholders expect it will evolve. This allows improvements to the approach whilst building mutual respect, meaning consumers feel more a part of the team. While living consumer engagement presents considerable opportunities, it shouldn't lessen the importance of co-designing the approach or aspiring to meet the principles of best practice throughout.

9.2.3 Larger groups of consumers may be beneficial

Consumers (like guideline developers) in our living guidelines found the unanticipated and fluctuating volume of work and its pace, and the frequent meetings at short notice were challenging. Conversely, in one guideline the volume and complexity of the work were much reduced in living mode.

Guideline developers and consumers described that involving more than 10 consumers in a consumer panel model allowed for wider consumer input; the formation of writing groups with equivalent numbers of consumers and clinicians; offered peer support to consumers; allowed upskilling of less experienced members, and the flexibility to cover scheduling difficulties.

In a living approach, guideline developers can start with a small group of consumers and grow as needed over time.

9.2.4 Consider starting with experienced and enthusiastic consumers

In our living guidelines, we found that initially involving experienced, responsive and enthusiastic consumers who could make an active contribution and get up to speed quickly was valuable. Careful selection criteria and adequate recruitment time would be necessary to support this, however, such skills may also develop with experience and the living approach allows such consumers to mentor new and/or less experienced consumers.

9.2.5 Plan for and manage renewal

Given the underdetermined period in which a guideline may be living, guideline developers should expect that consumers may prefer to make a time-limited commitment, and/or may cease their involvement at any time as their circumstances change.

This has resource implications with recurring recruitment activities, devising new processes, providing additional training and support, and ensuring clear (and ideally mutually agreed) expectations for new and continuing consumers. Creating online resources would offset the costs of repeated training but some 'live' training may still be needed. This also provides an opportunity to engage in succession planning, particularly if there are different tasks or roles (e.g. co-chairing) for consumers with particular skills or experience.

9.2.6 Ongoing training and support needs

The pace of activities with living guidelines, and the need to involve larger numbers of all guideline contributors means it is likely at least some consumer activities will be online. As such, we found it important to facilitate opportunities for consumers to get to know each other at the outset and connect informally throughout. In addition, consumers should be offered ongoing technical and other support and may value repeated or additional training.

Attention to consumers' support needs may be even more important in living guidelines, given the approach is suited to emerging conditions, whereby consumers' experience with the condition may be very recent. In addition, remuneration is particularly important in living guidelines, given the tight timeframes and changeable meeting times.

9.2.7 Living evaluation to inform improvements

Guideline developers and consumers highlighted that consumer engagement may be optimised if it is also viewed as living. Thus, all parties expect that it would evolve, in response to regular feedback. These could be informal evaluations (e.g., regular check-ins or brief surveys) or part of a wider guideline process evaluation. This may build mutual respect and mean consumers feel more a part of the team.

9.3 Example approaches: how consumers can be engaged in living guidelines

9.3.1 General processes for consumer engagement

In two guidelines, the engagement approach was devised with individual consumers (Stroke, AUS COVID-19) and via a partnership with an organisation representing consumers (AUS COVID-19). Consumers were recruited using a comprehensive screening and selection process from a pool of consumer representatives (AUS COVID-19, UK COVID-19, Stroke) or via the networks of guideline developers (Diabetes, Inflammatory arthritis).
In all guidelines, consumers were offered guidance and support, including an orientation to their role (AUS COVID-19, UK COVID-19, Stroke), guideline-specific training (i.e. GRADE; AUS COVID-19, Stroke, Diabetes, Inflammatory arthritis), ongoing informal support (including with technical queries; all guidelines), pre-meeting discussions (AUS COVID-19, UK COVID-19) and flexibility in methods or accessibility accommodations (e.g., live captioning online meetings; AUS COVID-19, UK COVID-19, Stroke). Consumers receive financial compensation in all guidelines except for the diabetes guideline, via attendance or sitting fees (AUS COVID-19, UK COVID-19, Inflammatory arthritis) or reimbursement of expenses, or a gift and certificate of appreciation (Stroke).

In all guidelines, developers and/or meeting facilitators were described as experienced and skilled in consumer engagement. The Inflammatory arthritis guideline team were the sole developer to undertake training in consumer engagement, while all guideline developers except in the diabetes guideline identified significant in-house expertise. In three guidelines (AUS COVID-19, Stroke, Inflammatory arthritis), process and impact evaluations (including consumers) have been conducted or are planned.

Three guidelines (UK COVID-19, Stroke, Inflammatory arthritis) include consumers from diverse backgrounds, corresponding to the PROGRESS-PLUS categories of place of residence (i.e., living in a regional area or less privileged area), race/culture/ethnicity/language, and disability.

9.4 Approaches to consumer engagement

Consumer panel (and GDG members)

In two guidelines (AUS COVID-19, Stroke), consumer input is provided via a Consumer Panel; a group of consumers, most of whom have lived experience of the relevant condition. In addition, one to two consumers from both Panels are full members of the Steering Group or GDG, acting as a bridge between the groups.
In the AUS COVID-19 guidelines, the eight-member Panel meets two-monthly (initially it was fortnightly) via videoconference in 90-minute meetings led by consumer co-chairs. They generate new questions, topics, and outcomes, and provide feedback on draft recommendations, with their decisions tabled at subsequent GDG meetings. In the stroke guidelines, the 28-member Consumer Panel is emailed draft summaries of relevant guideline sections (e.g., patient values and preferences; practical considerations) that align with their nominated interest areas. Panel members provide feedback over email, with all feedback reviewed by guideline developers. They also produce consumer versions of finalised recommendations via writing groups with clinicians, meeting by video or phone.

Consumers as GDG members

The other three guidelines (UK COVID-19, Diabetes, Inflammatory arthritis) include two to three consumers with lived experience of the relevant condition as GDG members. In the UK COVID-19 guidelines, the GDG diarises weekly online meetings, but only convenes them as needed. In the Inflammatory arthritis guidelines, the GDG meets as needed, depending on the recommendation (to date, this has been approximately monthly), and the diabetes guidelines GDG meets approximately every two months (but was more frequent initially). In these guidelines, consumers contribute to all aspects of guideline development, participating in meetings and out-of-session email discussions. Both diabetes and inflammatory arthritis guidelines include a consumer in the guideline oversight or steering committee.

10 Approval, publication, and dissemination of living guidelines

10.1 Approval process

Guideline developers may adopt several models for the approval process of recommendations and the publication of guideline updates. The approval process is highly dependent on the structure and governance of the participating organisations (e.g. Royal Colleges, Specialty organisations or consumer organisations) and therefore, there is no unique, universal approval process that could work for every guideline. However, developers and organisations are encouraged to discuss early the appropriate governance structure for a living guideline given that having a complex or time-consuming process for ratification and approval may hinder the whole purpose of living guidelines. For example, guideline developers may have gone through the whole process up to recommendation creation, but the last step (having all the required sign-offs) delays approval and publication.

Living guidelines must consider using electronic and virtual communication tools (such as virtual meetings, email chains, and/or messaging platforms) to allow swift and convenient approval and decision processes.

10.2 Governmental agencies and guideline regulatory bodies

Developing a living guideline does not preclude seeking the appropriate approvals from governmental bodies. Contacting and establishing links early with Guideline regulatory bodies (such as NHMRC) is crucial, given that the approval and review cycle of living guidelines may not fit the standard processes of these agencies.

10.3 Direct and indirect approval and publication

Guideline developers may choose between a more "direct" or "indirect" approach to recommendation approval and publication. Between these two options, a gradient of either more direct or indirect processes may be chosen. Developers need to bear in mind the balance between setting up a process that is more "rapid" vs. one that is slower but with more opportunity for feedback and consultation.

Direct approach

In a direct approach to recommendation approval and publication**,** recommendations are signed off after they have been crafted and agreed upon by the developers and panel, with the potential for an additional step consisting of an overseeing organisation's sign-off. In this direct model, swiftness prevails: the recommendation is generally published quicker, but with fewer opportunities for incorporating feedback from external agents.

Indirect approach

By contrast, a more indirect approach to recommendation approval and publication would rely on one or several rounds of internal and/or external public consultation before definitive sign-off. This model resembles the approval process of a traditional guideline and while it can take longer to develop, it offers more opportunities for input and feedback.

10.4 Publication and version control

Publication

Once a guideline and/or new/updated recommendations have been signed off by all relevant stakeholders, they can be published, preferably in an electronic format. Platforms such as MAGICApp allow both the development and publication of recommendations, with options to generate a PDF version of the guideline that can be exported and shared.

Version control

When a new version of a guideline is created, developers need to indicate any new, added, updated, or modified content so that the reader can easily acknowledge the amended information. Having visual cues as well as a changelog (a document or a section that describes and compiles the changes from the previous versions) associated with each version may help to achieve this.

A new version of the living guideline should also be identified to avoid users confusing it with a previous one. To clarify changes and help readers identify clearly which version of the guideline they are using, developers may choose a model similar to that of software production where a "major" version of the guideline is identified by an integer number (1.0 - 2.0 and so on) whereas a minor version is identified with a decimal number (2.1 - 2.2) indicating minor changes to the guideline.

Major versus minor changes

Currently, there is no "standardised" approach that defines what is considered a major or a minor change. However, as a general approach, when a guideline update contains at least one new recommendation or a major change to one of the existing recommendations (change in strength or direction) it could be considered sufficient to qualify as a "major" update. By contrast, minor changes to the evidence base (e.g. updated search, new study included without a change to recommendation or minor word editing and refining) could be considered minor changes.

Depending on the model for approval of a given living guideline, several "versions" of the guideline may coexist at the same time. This is particularly true in the case of modes of approval that follow a "public consultation" process, where an "approved" version of the guideline coexists with a "draft" version that is also available to the public. Developers should indicate to users clearly which of the versions they are accessing to avoid confusion.

10.5 Dissemination

Equally important for living guidelines is the development of effective dissemination channels, which may include the guideline presence in both traditional and social media, including X, Facebook, YouTube and similar social network sites. The release of a minor or major update should be accompanied by a communication release that helps the target users, as well as broader audiences, identify and access the new recommendations.

11 Maintenance phase

11.1 Preparing for maintenance phase/ "sustain" mode

After the initial recommendations have been developed, the second phase of development starts. It involves less frequent evidence surveillance, updates and meetings, which will only occur in response to any shift in priorities, or the emergence of new evidence.

This process is different from an existing guideline which has transitioned to "living" mode, as most of the recommendations will start in this "maintenance phase" with a few high-priority updates.

11.2 Revising topics and priority questions

After initial publication, a process of ongoing monitoring and revising topics and questions commence. This can be done continually or by establishing predetermined checkpoints for the review of priorities. Revising can use the same criteria as previously described in identification:

- Monitoring existing guidelines from other organisations for any updates or changes in priority levels.
- Monitoring of social media and mass media, for arising topical issues
- Evidence, from searches to inform the guideline scope, ongoing broad guideline searches, alerted to by stakeholders or the monitoring of clinical trial registries.
- Engagement with stakeholders, including guideline panels, healthcare consumers, and health professionals.
- Suggestions from the general public, via a website, communications team, or social media presence.
- Monitoring social media, mass media, and crowdsourcing, for relevant topical issues.
- Monitoring contextual, political, regulatory or other factors, such as new therapies seeking regulatory approval.
- New data showing potential biological plausibility of treatment effect modifiers, such as in vitro data.

11.3 De-prioritisation of topics and questions

Decisions surrounding when to de-prioritise a question may use the same criteria as selecting a question for living mode.

1) they are no longer deemed a high priority for decision-making;

2) the evidence underpinning them has reached a level of saturation and its certainty is unlikely to change;

3) no new evidence is expected to emerge

There may also be the need to de-prioritise if resourcing or funding levels change and the team can no longer maintain all the previously selected questions in living mode.

11.4 Updating guideline governance and guideline processes

During this phase to adapt to the ongoing needs of the prioritised, living questions, guideline developers may consider introducing changes in the governance structure, as well as other parts of the developing process. Examples of this include the frequency of panel meetings, the structure and capacity of the developing team or the processes surrounding guideline updates and approval. For instance, it may be decided to hold panels less frequently or move into an "as needed" meeting frequency. Similarly, such as in the case of NC19CET, recommendation crafting and approval can move from one specific panel to a more general panel (in that case the Guideline Leadership Group).

11.5 Long-term maintenance

Living guidelines are still in their early days so determining the best ways to achieve long-term maintenance is still an open question. Planning for the future from the beginning, with certain flexibility in the structure and in the modes in which the guideline is developed, may help to achieve long-term success. Equally, ensuring panel and member engagement is key for guideline developers, especially given that participating in a living guideline does not have a "finish date" and some participants (e.g. panellists) may feel overwhelmed or become disengaged over time. Guideline developers must consider that participants of a guideline can evolve and prepare mechanisms to find new collaborators if/as required.

Similarly, understanding how funding is going to support the living guideline process, and for how long, needs to be addressed from the beginning, as having uncertainty surrounding funding may impede the living guideline development process.

A potential way to address funding issues is to establish large partnerships, as well as engage in international collaboration so the endeavour of the living guideline is maintained by a larger body and the "burden" of its development is also shared across partners and organisations. Equally, international developers may successfully collaborate in the evidence appraisal and synthesis of a living guideline and sharing these avoids duplicity and research waste. This may finally allow (to follow an "old motto" of guideline development) the combination of "global evidence" with "local adaptation" and guidance.

11.6 Transitioning a living guideline out of living mode

Although we envisage that living guidelines are a feasible, long-term strategy for guideline developers and organisations, at some point, it may become appropriate in some circumstances to "wrap up" and stop the living process. In this case, developers need to indicate clearly that the guideline, and/or the topic, is no longer "living", the period that the guideline (or question) was maintained in living mode needs to be reflected, and the new update mode for a given guideline (or question) needs to be provided.

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